

AND THE USE THEREOF TO DESIGN OR IDENTIFY ANTIBACTERIAL AGENTS

Cross Reference Related to Related Applications

[0001] This application relates to U.S. Provisional Serial No. 60/372,095, filed on April 15, 2002 and which is incorporated in their entirety by reference herein.

Field of Invention

[0002] The present invention relates to the identification of essential and important genes in *Pseudomonas aeruginosa*, and the use thereof in screening assays and diagnostic methods to identify, evaluate or design antibacterial agents useful for the treatment of *Pseudomonas* infections. Such agents are particularly useful in preventing and treating opportunistic infections in immunocompromised individuals and for treating and preventing pulmonary infections in patients having cystic fibrosis disease. Also disclosed is a Bayessian statistical model that may be utilized to increase the statistical confidence that any given gene identified using the disclosed methodology is essential.

Background of Invention

[0003] Pseudomonas aeruginosa is a versatile Gram-negative bacterium that is able to adapt to and thrive in many ecological niches, from water and soil to plant and animal tissues. The bacterium is capable of utilizing a wide range of organic compounds as food sources, thus giving it an exceptional ability to colonize ecological niches where nutrients are limited, such as soil, marshes and coastal marine habitats. Hardalo, C. & Edberg, S. C. Pseudomonas aeruginosa: assessment of risk from drinking water. Crit. Rev. Microbiol. 23, 47-75 (1997). It also forms biofilms on wet surfaces such as those of rocks and soil. Costerton, J. W., Stewart, P. S. & Greenberg, E. P. Bacterial biofilms: a common cause of persistent infections. Science 284, 1318-1322 (1999). Ahearn, D. G., Borazjani, R. N., Simmons, R. B. & Gabriel, M. M. Primary adhesion of Pseudomonas aeruginosa to inanimate surfaces including biomaterials. Methods Enzymol. 310, 551-557 (1999). Analysis of the P. aeruginosa

genome has identified genes involved in locomotion, attachment, transport and utilization of nutrients, antibiotic efflux, and two component and other regulatory systems involved in sensing and responding to environmental changes. Because its natural habitat is the soil, where it exposed to bacilli, actinomycetes and molds, it has developed resistance to a variety of their naturally-occurring antibiotics.

[0004] The emergence of P. aeruginosa as a major opportunistic human pathogen during the past century may be a consequence of its resistance to the antibiotics and disinfectants that eliminate other environmental bacteria. P. aeruginosa is now a significant source of bacteraemia in burn victims, urinary-tract infections in catheterized patients, and hospital-acquired pneumonia in patients on respirators. Bodey, G. P., Bolivar, R., Fainstein, V. & Jadeja, L. Infections caused by *Pseudomonas* aeruginosa. Rev. Infect. Dis. 5, 279-313 (1983). It is also the predominant cause of morbidity and mortality in cystic fibrosis patients, whose abnormal airway epithelia allow long-term colonization of the lungs by P. aeruginosa. Thus, people with cystic fibrosis, burn victims, individuals with cancer and AIDS, and patients requiring extensive stays in intensive care units are particularly at risk of disease resulting from P. aeruginosa infection. P. aeruginosa is also a cause of a variety of different disorders including septicemia, urinary tract infections, pneumonia and chronic lung infections, endocarditis, dermatitis, osteochondritis, ear and eye infections, bone and joint infections, gastrointestinal infections and skin and soft tissue infections, including wound infections, pyoderma and dermatitis.

[0005] Cystic fibrosis is one of the most common fatal genetic disorders in the United States, affecting about 30,000 individuals. A comparable number of people in Europe also have CF. It is most prevalent in the Caucasian population, occurring in one of every 3,300 live births. The gene involved in cystic fibrosis was identified in 1989 and codes for a protein called the cystic fibrosis transmembrane conductance regulator (CFTR). This protein, normally produced in a number of tissues throughout the body, regulates the movement of salt and water in and out of these cells. One hallmark of CF is the presence of a thick mucus secretion that clogs the bronchial tubes in the lungs and plugs the exit passages from pancreas and intestines, leading to loss of function of these organs and resulting in a predisposition toward chronic bacterial infections.

Pseudomonas aeruginosa, having a propensity to live in warm, wet environments, is a particular problem for CF patients, whose lungs typically become colonized (inhabited long-term) by P. aeruginosa before their 10th birthday. Although antibiotics can decrease the frequency and duration of these attacks, resistant bacteria are quick to develop and the bacteria are never completely eradicated from the lung. More effective antibiotics are necessary for improving lung function and quality of life for CF patients for extended time periods.

[0006] Pseudomonas aeruginosa is notorious for its resistance to antibiotics and is, therefore, a particularly dangerous and dreaded pathogen. Todor, K. 2000 Pseudomonas aeruginosa, University of Wisconsin-Madison, http://www.bact.wisc.edu/microtextbook/disease/ pseudomonas.html, available on April 25, 2001. The permeability barrier afforded by its outer membrane LPS also contributes to its natural antibiotic resistance, as do the presence of two antibiotic resistance plasmids, both R-factors and RTFs, which are commonly transferred between cells by the bacterial processes of transduction and conjugation. Only a few antibiotics are effective against Pseudomonas, including tobramyocin (TOBI; Chiron), fluoroquinolone, gentamicin and imipenem, and even these antibiotics are not effective against all strains.

[0007] Pseudomonas aeruginosa disease generally begins with some alteration or circumvention of normal host defenses and may involve several different virulence determinants. Todor, 2000, supra. The ultimate Pseudomonas infection may be seen as composed of three distinct stages: (1) bacterial attachment and colonization; (2) local invasion; (3) disseminated systemic disease. Particular bacterial determinants of virulence mediate each of these stages and are ultimately responsible for the characteristic syndromes that accompany the disease. For instance, Pseudomonas utilize fimbriae or pili to adhere to the epithelial cells, apparently via binding to specific galactose or mannose or sialic acid receptors on epithelial cells. Fimbrial adherence may be an important step in Pseudomonas keratitis and urinary tract infections, as well as infections of the respiratory tract. Mucoid strains, which produce an a exopolysaccharide (alginate) have an additional or alternative adhesin which attaches to

the tracheobronchial mucin (N-acetylglucosamine). Therefore, mucoid strains of *P. aeruginosa* are commonly seen in lung infections.

[0008] The ability of *P. aeruginosa* to invade tissues depends upon its resistance to phagocytosis and the host immune defenses, and the extracellular enzymes and toxins that break down physical barriers and otherwise contribute to bacterial invasion. Todor, 2000, *supra*. For instance, *Pseudomonas e*lastase cleaves collagen, IgG, IgA, and complement, and also lyses fibronectin to expose receptors for bacterial attachment on the mucosa of the lung. Alkaline protease interferes with fibrin formation and lyses fibrin. Together, elastase and alkaline protease destroy the ground substance of the cornea and other supporting structures composed of fibrin and elastin. Elastase and alkaline protease together are also reported to cause the inactivation of gamma Interferon (IFN) and Tumor Necrosis Factor (TNF).

[0009] P. aeruginosa produces three other soluble proteins involved in invasion, including a cytotoxin (MW 25,000) and two hemolysins. Todor, 2000, supra. The cytotoxin is a pore-forming protein originally named leukocidin because of its effect on neutrophils, but it appears to be cytotoxic for most eukaryotic cells. Of the two hemolysins, one is a phospholipase and the other is a lecithinase. They appear to act synergistically to break down lipids and lecithin. The cytotoxin and hemolysins contribute to invasion through their cytotoxic effects on eukaryotic cells.

[0010] Pseudomonas aeruginosa also produces two extracellular protein toxins, Exoenzyme S and Exotoxin A. Exoenzyme S may act to impair the function of phagocytic cells in the bloodstream and internal organs to prepare for invasion by P. aeruginosa, and is typically produced by bacteria growing in burned tissue. Exotoxin A is partially identical to diphtheria toxin, and exhibits a necrotizing activity at the site of bacterial colonization and is thereby thought to contribute to the colonization process. Indirect evidence involving the role of exotoxin A in disease is seen in the increased chance of survival in patients with Pseudomonas septicemia that is correlated with the titer of anti-exotoxin A antibodies in the serum.

[0011] While therapeutic measures aimed at any of the above virulence factors may help to slow the progression of an infection and may be useful in combined therapeutic

regimens, given the variety of virulence factors of *P. aeruginosa*, antibacterial agents that inhibit growing bacteria by interacting with essential genes and essential gene products are necessary. Although, this is not to say that genes encoding virulence factors would not be essential to survival in particular niches or environments, emphasizing the importance of screening for gene essentiality in various pathogenic environments. *See, e.g.*, Coulter et al., 1998, *Staphylococcus aureus* genetic loci impacting growth and survival in multiple infection environments, Mol. Microbiol. 30(2): 393-404. However, as *P. aeruginosa* becomes more and more resistant to existing antibacterial agents, new compounds are required.

[0012] Indeed, reports of bacterial strains resistant to the most powerful known antibiotics are becoming more common, signaling that new antibiotics are needed for all bacteria, not only *P. aeruginosa*. For instance, the United States Center for Disease Control recently announced that one of the most powerful known antibiotics, vancomycin, was unable to treat an infection of *Staphylococcus aureus* (staph), an organism commonly found in the environment and responsible for many nosocomial infections. If this trend continues, some have warned that we could return to a time when a common bacterial infection is a life threatening matter. *See* Zyskind et al., WO 00/44906, published August 3, 2000.

[0013] Historically, however, the identification of new antibacterial drugs has been painstaking and laborious with no guarantee of success. Traditional methods involve blindly and randomly testing potential drug candidate molecules, with the hopes that one might be effective. Today, the average cost to discover and develop a new drug is nearly \$500 million, and the average time is 15 years from laboratory to patient. New identification and screening methods that shorten and improve this process are much needed.

[0014] A newly emerging technique for identifying new antibacterial agents is to first identify gene sequences and proteins required for the proliferation of bacteria, or "essential" genes and proteins, and then conduct a biochemical and structural analysis of that target gene or protein in order to derive compounds that interact with the target. Such methodology employs molecular modeling techniques, combinatorial chemistry

and other means to design candidate drugs, and offers a more directed alternative to merely screening random compounds with the hope that one might be suitable for a particular bacterium.

[0015] Nevertheless, even this preferred approach presents obstacles including the identification of essential genes and proteins, and the design of new assays for the genes thus identified in order to efficiently screen candidate compounds. Several groups have proposed systems for the identification of essential genes. For instance, Zyskind and colleagues propose a method of identifying essential genes in Escherichia coli by subcloning a library of E. coli nucleic acid sequences into an inducible expression vector, introducing the vectors into a population of E. coli cells, isolating those vectors that, upon activation and expression, negatively impact the growth of the E. coli cell, and characterizing the nucleic acid sequences and open reading frames contained on the subclones identified. See WO 00/44906, herein incorporated by reference. The disadvantage of this method is that the overexpression of nonessential genes can also negatively impact the cell, particularly the overexpression of membrane proteins and sugar transport proteins that are not necessary for growth where alternative carbon sources exist. Such proteins typically become trapped in membrane export systems when the cell is overloaded, and would be identified by this methodology. See Muller, FEMS Microbiol. Lett. 1999 Jul 1;176(1):219-27.

[0016] Another group proposes the identification of growth conditional mutants, and more specifically temperature sensitive (ts) mutants, as a means to identify essential genes in *Staphylococcus aureus*. *See* Benton et al., U.S. Patent 6,037,123, issued March 14, 2000, herein incorporated by reference. Each gene is identified by isolating recombinant bacteria derived from growth conditional mutant strains, i.e., following introduction of a vector containing a library of nucleic acid sequences, which would grow under non-permissive conditions but which were not revertants. These recombinant bacteria were found to contain DNA inserts that encoded wild type gene products that replaced the function of the mutated gene under non-permissive growth conditions. By this method, Benton and colleagues were able to identify 38 loci on the *S. aureus* chromosome, each consisting of at least one essential gene.

[0017] The disadvantages of this method are first, the chemical employed to induce mutagenesis (diethyl sulfate, DES) is capable of causing several mutations in the same cell, thereby complicating interpretation of the results. Second, the method is particularly labor intensive in that one must painstakingly analyze replica plates of individual colonies grown at permissive and non-permissive temperatures, where replica plates include both mutant and non-mutant cells. Thus, employing the appropriate level of mutagen to achieve a balance between minimizing the number of non-mutant colonies one must screen in order to identify one mutant, while at the same time avoiding multiple mutations in the same cell, may be an arduous task.

[0018] Another group has proposed a transposon mutagenesis system for identifying essential genes called "GAMBIT" ("genomic analysis and mapping by in vitro transposition"), and has used the system to identify essential genes first in the gram positive bacteria Haemophilus influenzae and Streptococcus pneumoniae, and more recently in Pseudomonas aeruginosa. See Akerley et al., Systematic identification of essential genes by In vitro mariner mutagenesis, Proc. Natl. Acad. Sci USA 95(15): 8927-32; Wong and Mekalanos, 2000, Proc. Natl. Acad. Sci. USA 97(18): 10191-96; and Mekalanos et al., U.S. Patent No. 6,207,384, issued March 27, 2001, herein incorporated by reference. GAMBIT involves first isolating and purifying specific genomic segments of approximately 10 kilobases using extended-length PCR, and creating a high density transposon insertion map of the isolated region using Himar1 transposon mutagenesis. The transposon insertions are then transferred to the chromosome following transformation of the bacteria with the transposon containing vectors, and selection for the antibiotic resistance marker on the transposon. The position of each transposon insertion with respect to a given PCR primer is then determined by genetic footprinting, i.e., by amplifying sub-PCR products using one of the original PCR primers and a primer that recognizes an internal site in the Himar 1 transposon. By analyzing the length of PCR fragments thus identified, it is possible to identify regions that are devoid of transposon insertions, thereby signaling regions that might contain essential genes.

[0019] While the GAMBIT method is a good technique for looking at a small region of the genome for essential genes, it would be extremely labor intensive to use this

method for analyzing the entire genome. This is particularly true for *P. aeruginosa*, whose genome (~6 megabases) is about 70% greater in size than the *H. influenzae* genome (~1.8 megabases). Furthermore, GAMBIT would not be readily applicable to use in organisms that are less recombinogenic than *H. influenzae*. Indeed, while the *H. influenzae* genome contains about 1700 protein coding genes, *P. aeruginosa* contains about 5570. According to U.S. Patent 6,207,384, one would need to clone and mutagenize the 6 million base pair genome of *P. aeruginosa* in 10,000 base pair fragments, isolating and characterizing 400-800 mutants per 10,000 base pair fragment. Generating 6 X 10⁵ mutants and characterizing them via PCR on gels would require a significant investment of labor, materials and time.

[0020] Another group at Abbott Laboratories has proposed a genome scanning method for identification of putative essential genes in *H. influenzae*, whereby random transposon insertions are mapped and analyzed to identify open reading frames containing no insertion in order to identify putative essential genes. Reich et al., 1999, Genome Scanning in *Haemophilus influenzae* for Identification of Essential Genes, J. Bacteriol. 181(16): 4961-68. However, even though transposon insertions were isolated that spanned the whole genome, the authors employed a genomic footprinting technique similar to that used in GAMBIT to map insertions in a short contiguous region of the chromosome. The method further employs the methods of mutation exclusion and zero time analysis in order to monitor the fate of individual insertions after transformation in growing culture, which looks at individual insertions on a case-by-case basis. Again, such techniques would be extremely labor-intensive for the *P. aeruginosa* genome, which is 70% larger than the genome of *H. influenzae*.

[0021] Wong and Mekalanos also proposed identifying essential genes in P. aeruginosa by starting with the knowledge of three essential genes in H. influenzae and using genetic footprint analysis to determine if the homologues of these genes are essential in P. aeruginosa. Of three homologues tested, only one was unable to accommodate a transposon insertion. See Wong and Mekalanos, supra. Such results underscore the fact that a gene that is shown to be essential in one species will not necessarily be essential in another, given that some gene products may fulfill different functional roles in different species. Furthermore, given the larger coding capacity of

the *P. aeruginosa* genome relative to that of other bacteria, it would not be surprising for *P. aeruginosa* to possess an increase in redundant gene functions, thereby decreasing the actual number of essential genes, and making them more difficult to identify.

[0022] Another method is entitled Transposon Mediated Differential Hybridisation (TMDH), which is disclosed in WO 01/07651, herein incorporated by reference. This method entails (i) providing a library of transposon mutants of the target organism; (ii) isolating polynucleotide sequences from the library which flank inserted transposons; (iii) hybridising said polynucleotide sequences with a polynucleotide library from said organism; and (iv) identifying a polynucleotide in the polynucleotide library to which said polynucleotide sequences do not hybridise in order to identify an essential gene of the organism. However, the problem with this methodology is that it has a high propensity to lead to false positives, and many essential genes will be missed. Furthermore, the method does not yield any detailed information regarding the loci disrupted by transposons, or whether they were hit more than once.

[0023] Thus, there is a great need for more efficient methods to identify essential genes, particularly in *P. aeruginosa*, so that new antibacterial agents may be designed therefrom for use in treatment of *P. aeruginosa* infections.

Summary of Invention

[0024] The present inventors have devised a database of potential essential or otherwise important genes in *P. aeruginosa*, which may be used to verify essentiality and design antibacterial agents active against the targets thus identified. In particular, the inventors have isolated and mapped a library of at least about 5,000 to at least about 14,000 transposon insertions in the genome of *P. aeruginosa*, and more preferably a library of at least about 14,000 transposon insertions, and even more preferably a library of at least about 10,000 to at least about 14,000 transposon insertions, using the recently published *P. aeruginosa* gene sequence. The map thus generated was used to form a database of approximately 1500 to 3000 open reading frames, or more preferably about 1500 to 2000 open reading frames, for which no transposon insertions could be obtained, each of which possibly represents an essential

gene required for growth and proliferation of *P. aeruginosa* on rich media, or an important gene, the mutation of which results in an attenuated growth mutant. Also disclosed is a Bayessian statistical model that may be utilized to increase the statistical confidence that any given gene identified using the disclosed methodology is essential.

Thus, one aspect of the invention is a database of putative essential or [0025] otherwise important genes, defined by the absence of transposon insertions in those genes in a High Throughput Transposon Insertion Map (HTTIM) database comprising about 10,000 to about 14,000 transposon insertions in the genome of Pseudomonas aeruginosa. Minimally, such a database comprises approximately 1800 open reading frames (ORFs), each of which may be further tested for essentiality using a variety of tests disclosed herein. However, predictions of essentiality or importance may be bolstered based on length of the ORF and predicted function and other statistical factors, thereby providing for more narrow databases of putative essential genes. Thus, the invention also includes databases that are more narrow and comprise only those genes for which essentiality or importance may be predicted with at least an 80% confidence level, and include at least about 850 to about 875 genes. The invention also includes databases assigned a confidence level of about 85% and including at least about 675 to about 700 genes. The invention further includes databases assigned a confidence level of about 90% including at least about 475 to about 500 genes. Further, the invention includes databases assigned a confidence level of about 95% and including at least about 200 to 250 genes.

[0026] The transposon insertion map and database of putative essential or otherwise important open reading frames (ORFs) obtained may be used to confirm the essentiality or importance of genes, for example by integration knock outs in the presence of chromosomal complementation or by integration and activation of a regulatable promoter. An "essential" gene is one that cannot be "knocked out," i.e. for which null mutants having complete absence of the gene product are not viable. This does not mean, however, that such genes could not tolerate point mutations or truncations that preserve sufficient gene product function so as to enable cell growth and survival. Essential genes are to be distinguished from "important" genes, which are also included in the present invention, in that a "knock out" of an important gene does not lead to cell

death but rather results in an attenuated growth mutant. Such genes may be included in the database of open reading frames not hit by random transposon mutagenesis as described herein, because attenuated growth colonies may be significantly smaller than the average *P. aeruginosa* colony and may have been overlooked when transposon insertion mutants were picked to generate the high throughput transposon insertion database (HTTIM).

[0027] Nevertheless, important gene products may interact with or regulate other genes, gene products or cellular processes that are essential, thereby making such gene products appropriate targets for drug design. Moreover, most drugs don't effectively kill all the pathogenic bacteria in the body; rather, they kill or growth attenuate a portion of the bacteria, empowering the immune system to target the remainder. Hence, important genes that, when targeted with an antibacterial agent, result in attenuated growth, are also targets for the antibacterial drugs of the present invention.

[0028] The invention also includes a database of attenuated growth mutants identified from the HTTIM transposon database. The genes marked by such mutations are of the same class of importance as the "important" genes identified in the no-hit database of genes, except that the growth attenuated nature of such transposon mutants was discovered at the transposon mutagenesis stage, rather than at the stage where essentiality is tested via targeted knock out. Thus, genes that when mutated confer attenuated growth may be identified from two sources: (1) from the library of open reading frames that did not receive a transposon insertion during HTTIM but were subsequently identified as an important gene when essentiality was tested via knock out and/or promoter swap strategies, and (2) from the HTTIM database itself when in the process of accumulating transposon insertion mutants it was observed that a particular insertion conferred an attenuated growth phenotype.

[0029] Such attenuated mutants grow more slowly than wild type, and may grow more slowly due to reduced expression of an essential gene, i.e., transposon is in gene that regulates expression of an essential gene, or due to expression of a truncated form of an essential gene, i.e., transposon is in the essential gene itself and leads to expression of a truncated mRNA. For example, mutants that show a higher drug

susceptibility could be the result of insertions in a gene that potentiates resistance, such an efflux pump, or due to reduced expression of essential genes involved in the mechanism of action of the drug. Expression of mutated forms of essential and important genes may make the cell more susceptible to compounds that inhibit that particular gene or gene product, and may allow the identification of antibacterial agents with greater sensitivity. Furthermore, screening in whole cells overcomes the potential problems of uptake and efflux that are sometimes an issue for compounds identified via enzyme-based assays.

[0030] The essential and important genes of the invention may be used to design, screen for and evaluate potential antibacterial agents for the purpose of developing new treatments for *P. aeruginosa* infection. Antibacterial agents identified according to the invention may have activity against the gene or against the corresponding gene product or metabolic pathways requiring the gene product. For instance, antibacterial agents according to the invention may include antisense nucleic acids or regulatory proteins that bind to open reading frames, to upstream polar sequences or to promoters that drive expression of the genes encoded by such open reading frames. Active agents according to the invention may also include antibodies or proteins that bind to proteins encoded by open reading frames, or to transcriptional or translational regulators of such genes or proteins, or to binding partners of such proteins. Agents may also be chemical compounds designed following molecular modeling of essential gene products according to the invention, or mutant proteins designed therefrom that compete with the essential wild type protein for reactive cell components or for interacting nutrients, as well as agents from random chemical.

[0031] The present invention therefore includes methods and assays for identifying antibacterial agents having specificity for the essential or important open reading frames identified, or to genes and proteins that interact with such open reading frames or the products encoded thereby. Once essential and important open reading frames are identified, antibacterial agents may be identified using the assays and methods described herein, or by any suitable assay. Such assays may vary depending on the function delineated for each essential locus, as would be apparent to those of skill in the art. For instance, enzyme assays may be designed based on the predicted function of

essential and important genes in order to define classes of inhibitors to be tested. Also, random chemical libraries may be screened for activity against the isolated genes or gene products. Cell lines may be designed or isolated that demonstrate reduced expression of essential genes, thereby providing a sensitive screening tool for inhibitors that effect the activity of that gene or gene product as it functions in the cell. Such cell lines may be devised from cells having transposon insertions that lead to attenuated growth, or may be constructed by the promoter swap techniques described herein, by using a regulatable promoter that can be used to increase gene expression, allowing for confirmation of target specificity. Here, the minimal inhibitory concentration of the inhibitor is directly related to the expression level of the target gene, such that under low expression, an attenuated growth cell is more susceptible to an inhibitor than the wild type strain, and as you raise the expression level, the minimum inhibitory concentration (MIC) increases. The MIC shift will be consistent when the inhibitor acts on the regulated target.

[0032] Active agents and compounds can be formulated into pharmaceutical compounds and compositions, effective for treating and preventing *Pseudomonas* infections in accordance with the methods of the invention. Such therapy will be particularly useful in the hospital setting for preventing and treating nosocomial infections, and for administering to cystic fibrosis patients to improve lung function and quality of life. Depending on the activity of the essential or important gene targeted, such agents could also be useful in treating all types of *Pseudomonas* infections ranging from bacteraemia and septicemia, urinary-tract infections, pneumonia and chronic lung infections, burn infections, cancer, AIDS, endocarditis, dermatitis, osteochondritis, ear and eye infections, bone and joint infections, gastrointestinal infections and skin and soft tissue infections, including wound infections, pyoderma and dermatitis. Further, the invention provides pharmaceutical compositions appropriate for use in methods of treating bacterial infections described above.

Brief Description of the Drawings

PCT/US02/35518

- [0033] Figure 1. Depiction of a single crossover recombination event resulting in integration of a plasmid into the bacterial chromosome. Isolation of such recombinants indicates that the targeted gene is not essential.
- [0034] Figure 2. Single crossover and integration of a plasmid resulting in the replacement of a wild type promoter with a regulatable promoter.
- [0035] Figure 3. Depiction of the 'promoter swap' strategy, using transformation of pBEM10 into *P. aeruginosa* in order to replace the *lpxC* promoter with the arabinose araBAD promoter, thereby allowing modulation of its *lpxC* expression by the use of a simple sugar, arabinose.
- [0036] Figure 4. Graph showing the susceptibility or non-susceptibility of various E. coli and P. aeruginosa strains to the inhibitor L161,240.
- [0037] Figure 5. Graph depicting the effect of tetracycline and L161,240 on the growth of *P. aeruginosa* strain PA01 with and without polymixin permeabilization.
- [0038] Figure 6. Sensitivity of various *E. coli* and *P. aeruginosa* strains to inhibitor L161,240 following promoter swap and transformation with vector expressing *E. coli* lpxC or *P. aeruginosa* lpxC. *E. coli* "swaps" refer to *P. aeruginosa* containing a vector comprising *E. coli* lpxC, and "PA swaps" refer to *P. aeruginosa* containing a vector comprising *P. aeruginosa* lpxC.
- [0039] Figure 7. Graph illustrating ORF coverage by Tn5 achieved in High-Throughput Transposon Insertion Mapping (HTTIM), wherein 30% of the genes in the genome are candidate essential genes where ORF size is not taken into account in predicting essentiality.
- [0040] Figure 8. Graph depicting the probability of identifying an essential gene given no transposon insertion, as a function of gene size.
- [0041] Figure 9. A circular map of the *P. aeruginosa* genome showing distribution of transposon insertion sites constituting a HTTIM of the invention, and demonstrating the

random nature of the transposon employed. The length of the bars radiating outward from the center of the circular map reflect the number of transposon insertions per non-overlapping kilobase.

- [0042] Figure 10. Histogram depicting the number of ORFs in the *P. aeruginosa* genome of (a) up to 4000 base pairs and (b) from 4000 up to 16884 base pairs.
- [0043] Figure 11. Graph showing likelihood and accumulative likelihood gains.
- [0044] Figure 12. Trajectory of the algorithm projected in a subspace spanned by two gene sizes. The x-axis represents genes of sizes 151-160 DNA base-pairs and y-axis represents genes of sizes 171-180 DNA base-pairs. Here n=(2,1) and M=(7,9). The median gene size of each group is used as the gene size. At iteration number 66, the likelihood gain is maximum in the direction of increasing the number of nonessential genes by one for genes with size 171-180 DNA base-pairs. At iteration number 443, the largest likelihood gain is obtained in the direction of increasing one nonessential genes for genes of sizes 151-160 DNA base pair. At any point, moving backwards has a negative likelihood gain.
- [0045] Figure 13. More trajectories of the searching algorithm projected in different subspaces.
- [0046] Figure 14. Plot of likelihood for different initial values.
- [0047] Figure 15. Trajectories of the algorithm with different starting values projected in the subspace spanned by two gene sizes: 1101-1150 DNA base-pairs for X-axis and 921-930 DNA base-pairs for y-axis.
- [0048] Figure 16. Top: (A) The top line is \vec{M} , number of genes, the bottom line is \vec{n} , the number of genes with at least one observed insertion; the line in the middle is \vec{N} , the number of estimated nonessential genes. For demonstration purpose, a cubic spline smooth is applied to the data. Bottom: Histogram of resamples of \hat{r} (B) and $\hat{\lambda}$ (C).
- [0049] Figure 17. Plot of \hat{N}_i/M_i . The doted line is the value of \hat{N}_i/M_i and the solid line is a moving average smooth.

[0050] The essential and important open reading frames identified in the present invention were originally part of a library of putative nucleic acid sequences generated from P. aeruginosa strains PA01 and PAK. See Table 1. Nevertheless, it is expected that the genes identified will also be essential or important in related P. aeruginosa strains as well as other *Pseudomonas* species, given the low sequence diversity that exists between P. aeruginosa strains of widely diverse environments and the pronounced structural and functional homology of gene products. See, e.g., Spangenberg et al., 1998, Structural and functional implications of sequence diversity of Pseudomonas aeruginosa genes oriT, ampC and fliC, Electrophoresis 19(4): 545-50; Ruimy et al., 2001, Genetic diversity of Pseudomonas aeruginosa strains isolated from ventilated patients with nosocomial pneumonia, cancer patients, bacteremia, and environmental water, Infect. Immun. 69(1): 584-8. For instance, comparative sequencing of several P. aeruginosa genes from several environmental and clinical isolates revealed the sequence diversity to be about one order of magnitude lower than in comparable housekeeping genes from Salmonella. See Kiewitz and Tummler, 2000, Sequence diversity of Pseudomonas aeruginosa: impact on population structure and genome evolution, J. Bacteriol. 182(11): 3125-35. Thus, it is expected that agents identified as antibacterial based on their interaction with genes or gene products of P. aeruginosa PA01 or PAK will be broadly applicable as antibacterial agents against a variety of *Pseudomonas* species as well as other bacteria including but not limited to Escherichia, Hemophilus, Vibrio, Borrelia, Enterococcus, Heliobacter, Legionella, Mycobacterium, Mycoplasma, Neisseria, Staphylococcus, Streptococcus, etc.

[0051] Thus, the present invention encompasses an isolated nucleic acid molecule comprising a nucleic acid sequence encoding a polypeptide having at least 80% sequence identity to a polypeptide encoded by a nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1. More preferably, the present invention encompasses an isolated nucleic acid molecule comprising a nucleic acid sequence encoding a polypeptide having at least about 85 to 90% sequence identity to a polypeptide encoded by a nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open

reading frames (ORFs) listed in Table 1. Even more preferably, the present invention encompasses an isolated nucleic acid molecule comprising a nucleic acid sequence encoding a polypeptide having at least about 90 to about 95% sequence identity to a polypeptide encoded by a nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1.

[0052] In particular, the invention encompasses isolated nucleic acid molecules comprising nucleic acid sequences encoding polypeptides having at least 80% sequence identity, or more preferably at least about 85 to 90 to 95% identity, to a polypeptide encoded by an essential or important nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1, wherein essentiality or importance of said nucleic acid sequence is determined by integration knock-out coupled with extra-chromosomal complementation. Likewise, the invention encompasses isolated nucleic acid molecules comprising nucleic acid sequences encoding polypeptides having at least 80% sequence identity, or more preferably at least about 85 to 90 to 95% identity, to a polypeptide encoded by an essential nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1, wherein essentiality or importance of said nucleic acid sequence is determined by integration of a regulatable promoter into the gene, or via any other suitable method.

[0053] In one embodiment, the polynucleotides of the invention are recombinant. Recombinant polynucleotides of the invention include proteins of genomic, cDNA, semisynthetic, or synthetic origin, which, by virtue of its origin or manipulation (1) is not associated with all or a portion of a polynucleotide with which it is associated in nature; (2) is linked to a polynucleotide other than that to which it is linked in nature; or (3) does not occur in nature.

[0054] Given that the library of nucleic acid sequences encompassed in Table 1 provides an unprecedented tool useful for the identification of essential and otherwise important genes in *Pseudomonas* and the construction and isolation of attentuated mutants, the present invention includes a library of nucleic acid sequences consisting essentially of nucleic acid sequences having at least 70% sequence identity, or more

preferably at least about 80 to 90 to 95% identity, to a nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1, wherein said library of nucleic acid sequences is employed to identify essential or otherwise important genes or to construct or isolate attenuated mutants in *Pseudomonas*.

[0055] Also encompassed in the invention is a map of at least about 10,000 to about 14,000 transposon insertions in the genome of *Pseudomonas aeruginosa* (High-Throughput Transposon Insertion Database or HTTIM), wherein said map is useful for identifying genes that are essential or important for survival of said *Pseudomonas aeruginosa*, i.e., by permitting the generation of a database of open reading frames that do not contain a transposon insertion. Figure 9 contains a circular map of the *P. aeruginosa* genome depicting 12,000 to 13,000 transposon insertion sites constituting a HTTIM of the invention, and demonstrates the random nature of the transposon employed. The length of the bars radiating outward from the center of the circular map reflect the number of transposon insertions per non-overlapping kilobase. Table 3 contains a list of 13,515 specific Tn5 transposon insertion sites generated in either PAK or PA01, with the 473 mutants 12516-13043 being identified as attenuated for growth.

[0056] Thus, the databases and libraries disclosed herein may be used to formulate useful subsets of these libraries and databases. Accordingly, the invention includes subsets of the databases and libraries disclosed. For instance, mutants 12516-13043 are identified as attenuated for growth and as such, the genes in this subset could be useful drug targets. Accordingly, this group of 473 mutants from the HTTIM database of 13,515 transposon hits provides a useful subset database for comparing homologies with essential genes of other organisms, for computer modeling of potential antibacterial agents, etc. A particularly useful database subset is one containing essential genes from *P. aeruginosa* that are also identified as essential in other Gram negative or Gram positive bacteria. Indeed, genes that have essential homologs in other bugs are likely to provide useful targets for broad spectrum antibacterial agents, i.e., agents that have broad spectrum activity as an antibacterial agent. Genes in the putative essential or important gene database have already been identified via BLAST

or other database analyses, and constitute an exemplary subset database of the present invention. See Table 4.

[0057] Further, the databases and subset databases of the present invention may also be used as comparative tools with other like databases or database subsets to identify broad spectrum. For instance, particularly envisioned is an embodiment wherein the database of putative essential and important genes identified in *P. aeruginosa* is cross-referenced with a similar database formed from *S. aureus*, wherein homologues present in both databases signal a potential target for a broad spectrum antibacterial agent. Cross-referencing between *P. aeruginosa* and *S. aureus* in particular will identify antibacterial targets for identifying broad spectrum antibiotics active against both Gram negative and Gram positive bacteria. However, databases derived from any bacteria could be employed in such comparisons, as well as databases formed from yeast, fungi, mycoplasma, and other potential pathogens.

[0058] Also encompassed in the invention is the use of essential and important genes and the corresponding proteins expressed thereto in the design of vaccines for eliciting prophylactic or therapeutic immune responses against *Pseudomonas aeruginosa*.

[0059] Such vaccines will typically comprise a *Pseudomonas aeruginosa* protein antigen or fragment or variant thereof encoded by an essential gene. Additionally, such antigens will preferably be a protein expressed on the surface of the bacteria.

[0060] Such vaccines will typically comprise a *Pseudomonas aeruginosa* protein antigen or fragment or derivative thereof encoded by an essential or important gene. Preferably, the protein antigen expressed from a recombinant polynucleotide.

[0061] Where the invention is directed to a fragment of a protein encoded by an essential or important gene, said fragment is preferably at least 8 to 12 amino acids long, and even more preferably at least about 20 to 30 amino acids long. Preferably, the fragment comprises either a B cell or a T cell epitope.

[0062] Where the invention is directed to a derivative of a protein encoded by an essential or important gene, said derivative contains one or more amino acid substitutions, additions or deletions. Preferably, the amino acid substitutions are

conservative amino acid replacements. Conservative amino acid replacements are those that take place within a family of amino acids that are related in their side chains. Genetically encoded amino acids are generally divided into four families: (1) acidic = aspartate, glutamate; (2) basic = lysine, arginine, histidine; (3) non-polar = alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan; and (4) uncharged polar = glycine, asparagine, glutamine, cystine, serine, threonine, tyrosine. Phenylalanine, tryptophan, and tyrosine are sometimes classified jointly as aromatic amino acids. For example, it is reasonably predictable that an isolated replacement of a leucine with an isoleucine or valine, an asparate with glutamate, a threonine with a serine, or a similar conservative replacement of an amino acid with a structurally related amino acid will not have a major effect on the biological activity. Polypeptide molecules having substantially the same amino acid sequence as the protein by possessing minor amino acid substitutions that do not substantially affect the functional aspects are encompassed with the scope of derivatives of the proteins of the invention.

[0063] The polypeptide fragment or derivative is preferably immunologically identifiable with the polypeptide encoded by the essential or important gene. The polypeptide fragment or derivative is preferably immunogenic and is able to cause a humoral and/or cellular immune response, either alone or when linked to a carrier, in the presence or absence of an adjuvant. The polypeptide fragment or derivative may be fused to or incorporated into another polypeptide sequence. This other polypeptide sequence may include one or more other proteins, fragments or derivatives thereof encoded by an essential or important gene. The other polypeptide sequence may also include a polypeptide sequence which allows for presentation of the polypeptide fragment or derivative.

[0064] Accordingly, the present invention encompasses an isolated polypeptide and fragments and derivatives thereof, wherein said polypeptide has at least 80% sequence identity to a polypeptide encoded by a nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1. More preferably, the present invention encompasses an isolated polypeptide and fragments and derivatives thereof, wherein said polypeptide has at least about 85 to 90% sequence identity to a polypeptide encoded by a nucleic acid sequence selected

from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1. Even more preferably, the present invention encompasses an isolated polypeptide and fragments and derivatives thereof, wherein said polypeptide has at least about 90% to about 95% sequence identity to a polypeptide encoded by a nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1.

[0065] In particular, the invention encompasses isolated polypeptides and fragments and derivatives thereof, wherein said polypeptides have at least 80% sequence identity, or more preferably at least about 85 to 90 to 95% identity, to a polypeptide encoded by an essential or important nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1, wherein the essentiality or importance of said nucleic acid sequence is determined by integration knock-out couple with extra-chromosomal complementation. Likewise, the invention encompasses isolated polypeptides and fragments and derivatives thereof, wherein said polypeptides have at least 80% sequence identify, or more preferably at least about 85 to 90 to 95% identity, to a polypeptide encoded by an essential nucleic acid sequence selected from the group consisting of the *Pseudomonas aeruginosa* open reading frames (ORFs) listed in Table 1, wherein essentiality or importance of said nucleic acid sequence is determined by integration of a regulatable promoter into the gene, or via any other suitable method.

[0066] Also encompassed in the invention are therapeutic and prophylactic vaccines that comprise ligands that specifically bind antigens encoded by essential or important genes identified according to the invention, for use in, for instance, passive immunization. Preferred ligands are antibodies and antibody fragments that specifically bind the antigen encoded by the essential gene. Such antibodies may be polyclonal or monoclonal. Types of antibodies and antibody fragments include by way of examples murine antibodies, chimeric, antibodies, humanized antibodies, Fab fragments, Fab₂ fragments and human antibodies and scFv's. Methods for producing antibodies and antibody fragments by recombinant and non-recombinant methods are well known to those skilled in the art. In some embodiments the antigen used in such

passive immunization may be attached to a cytotoxic moiety, e.g., a radionuclide or other agent that is cytotoxic against the bacteria.

[0067] Further encompassed within the scope of the invention are cells or viral vectors that express on their surface a Pseudomonas aeruginosa essential gene, fragment or variant identified according to the invention.

[0068] In the case of prophylactic vaccines, the vaccine will comprise an immunogenic composition comprising a prophylactically effective amount of an antigen, antibody, cells or vector expressing an antigen encoded by an essential or important gene and will be formulated such that upon administration it elicits a protective immune response. In the case of therapeutic vaccines, the vaccine will comprise an immunogenic composition comprising a therapeutically effective amount of an antigen, antibody, cells or vectors expressing an antigen encoded by an essential or important gene and will be formulated such that upon administration it elicits a therapeutic immune response. Dosage effective amounts of prophylactic and therapeutic vaccines will be determined by known methods and will typically vary from about 0.00001 g/kg body weight to about 5-10 g/kg body weight.

[0069] The immunogenic compositions of the invention can be administered by known methods, i.e., mucosally or parenterally.

[0070] Suitable routes of mucosal administration include oral, intranasal (IN), intragastric, pulmonary, intestinal, rectal, ocular, and vaginal routes. Preferably, mucosal administration is oral or intranasal.

[0071] Where mucosal administration is used, the immunogenic composition is preferably adapted for mucosal administration. For instance, where the composition is administered orally, it may be in the form of tablets or capsules (optionally entericcoated), liquid, transgenic plants, etc. Where the composition is administered intranasally, it may be in the form of a nasal spray, nasal drops, gel or powder. Where the antigen composition is adapted for mucosal administration, it may further be formulated such that the antigen remains stable, for instance by the use of carriers and excipients.

The immunogenic compositions of the invention can further comprise a mucosal adjuvant. Mucosal adjuvants suitable for use in the invention include (a) E.coli heat-labile enterotoxin ("LT"), or detoxified mutants thereof, such as the K63 or R72 mutants; (B) cholera toxin ("CT"), or detoxified mutants thereof; or (C) microparticles (i.e., a particle of ~100nm to ~150µm in diameter, more preferably ~200nm to ~30µm in diameter, and most preferably ~500nm to ~10µm in diameter) formed from materials that are biodegradable and non-toxic (e.g. a poly(α -hydroxy acid), a polyhydroxybutyric acid, a polyorthoester, a polyanhydride, a polycaprolactone etc.); (D) a polyoxyethylene ether or a polyoxyethylene ester (see International patent application WO 99/52549); (E) a polyoxyethylene sorbitan ester surfactant in combination with an octoxynol (see International patent application WO 01/21207) or a polyoxyethylene alkyl ether or ester surfactant in combination with at least one additional non-ionic surfactant such as an octoxynol (see International patent application WO 01/21152); (F) chitosan (e.g. International patent application WO 99/27960) and (G) an immunostimulatory oligonucleotide (e.g. a CpG oligonucleotide) and a saponin (see International patent application WO 00/62800). Other mucosal adjuvants are also available (e.g. see chapter 7 of Vaccine design: the subunit and adjuvant aproach, eds. Powell & Newman, Plenum Press 1995 (ISBN 0-306-44867-X).

[0073] Mutants of LT are preferred mucosal adjuvants, in particular the "K63" and "R72" mutants (e.g. see International patent application WO 98/18928), as these result in an enhanced immune response.

[0073] Microparticles are also preferred mucosal adjuvants. These are preferably derived from a poly(α -hydroxy acid), in particular, from a poly(lactide) ("PLA"), a copolymer of D,L-lactide and glycolide or glycolic acid, such as a poly(D,L-lactide-coglycolide) ("PLG" or "PLGA"), or a copolymer of D,L-lactide and caprolactone. The microparticles may be derived from any of various polymeric starting materials which have a variety of molecular weights and, in the case of the copolymers such as PLG, a variety of lactide:glycolide ratios, the selection of which will be largely a matter of choice, depending in part on the coadministered antigen.

[0074] Antigen may be entrapped within the microparticles, or may be adsorbed to them.

[0075] Entrapment within PLG microparticles is preferred. PLG microparticles are discussed in further detail in Morris et al., (1994), Vaccine, 12:5 – 11, in chapter 13 of Mucosal Vaccines, eds. Kiyono et al., Academic Press 1996 (ISBN 012410587), and in chapters 16 & 18 of Vaccine design: the subunit and adjuvant aproach, eds. Powell & Newman, Plenum Press 1995 (ISBN 0-306-44867-X).

[0076] LT mutants may advantageously be used in combination with microparticle-entrapped antigen, resulting in significantly enhanced immune responses.

[0077] Suitable routes of parenteral administration include intramuscular (IM), subcutaneous, intravenous, intraperitoneal, intradermal, transcutaneous, and transdermal (see e.g., International patent application WO 98/20734) routes, as well as delivery to the interstitial space of a tissue.

[0078] The immunogenic compositions of the invention may be adapted for parenteral administration (e.g., in the form of an injectable, which will typically be sterile and pyrogen-free).

[0079] The immunogenic composition may further comprise a parenteral adjuvant. Parenteral adjuvants suitable for use in the invention include: (A) aluminum compounds (e.g. aluminum hydroxide, aluminum phosphate, aluminum hydroxyphosphate, oxyhydroxide, orthophosphate, sulfate etc. (e.g. see chapters 8 & 9 of Vaccine design: the subunit and adjuvant aproach, eds. Powell & Newman, Plenum Press 1995 (ISBN 0-306-44867-X) (hereinafter "Vaccine design"), or mixtures of different aluminum compounds, with the compounds taking any suitable form (e.g. gel, crystalline, amorphous etc.), and with adsorption being preferred; (B) MF59 (5% Squalene, 0.5% Tween 80, and 0.5% Span 85, formulated into submicron particles using a microfluidizer) (see Chapter 10 of Vaccine design; see also International patent application WO 90/14837); (C) liposomes (see Chapters 13 and 14 of Vaccine design); (D) ISCOMs (see Chapter 23 of Vaccine design); (E) SAF, containing 10% Squalane, 0.4% Tween 80, 5% pluronic-block polymer L121, and thr-MDP, either microfluidized

into a submicron emulsion or vortexed to generate a larger particle size emulsion (see Chapter 12 of Vaccine design); (F) RibiTM adjuvant system (RAS), (Ribi Immunochem) containing 2% Squalene, 0.2% Tween 80, and one or more bacterial cell wall components from the group consisting of monophosphorylipid A (MPL), trehalose dimycolate (TDM), and cell wall skeleton (CWS), preferably MPL + CWS (DetoxTM); (G) saponin adjuvants, such as QuilA or QS21 (see Chapter 22 of Vaccine design), also known as StimulonTM; (H) ISCOMs, which may be devoid of additional detergent (International patent application WO 00/07621); (I) complete Freund's adjuvant (CFA) and incomplete Freund's adjuvant (IFA); (J) cytokines, such as interleukins (e.g. IL-1, IL-2, IL-4, IL-5, IL-6, IL-7, IL-12, etc.), interferons (e.g. interferon-γ), macrophage colony stimulating factor, tumor necrosis factor, etc. (see Chapters 27 & 28 of Vaccine design); (K) microparticles (see above); (L) monophosphoryl lipid A (MPL) or 3-Odeacylated MPL (3dMPL) (e.g. chapter 21 of Vaccine design); (M) combinations of 3dMPL with, for example, QS21 and/or oil-in-water emulsions (European patent applications 0835318, 0735898 and 0761231); (N) oligonucleotides comprising CpGmotifs (see Krieg (2000) Vaccine, 19:618 - 622; Krieg (2001) Curr. Opin. Mol. Ther., 2001, 3:15 – 24; WO 96/02555, WO 98/16247, WO 98/18810, WO 98/40100, WO 98/55495, WO 98/37919 and WO 98/52581, etc.) i.e. containing at least one CG dinucleotide, with 5-methylcytosine optionally being used in place of cytosine; (O) a polyoxyethylene ether or a polyoxyethylene ester (International patent application WO 99/52549); (P) a polyoxyethylene sorbitan ester surfactant in combination with an octoxynol (International patent application WO 01/21207) or a polyoxyethylene alkyl ether or ester surfactant in combination with at least one additional non-ionic surfactant such as an octoxynol (International patent application WO 01/21152); (Q) an immunostimulatory oligonucleotide (e.g. a CpG oligonucleotide) and a saponin (International patent application WO 00/62800); (R) an immunostimulant and a particle of metal salt (International patent application WO 00/23105); (S) a saponin and an oilin-water emulsion (International patent application WO 99/11241); (T) a saponin (e.g. OS21) + 3dMPL + IL-12 (optionally + a sterol) (International patent application WO 98/57659); and (U) other substances that act as immunostimulating agents to enhance the effectiveness of the composition (e.g. see Chapter 7 of Vaccine design).

[0080] Aluminium compounds and MF59 are preferred adjuvants for parenteral use.

[0081] The immunognic compositions of the invention may be administered in a single dose, or as part of an administration regime. The regime may include priming and boosting doses, which may be administered mucosally, parenterally, or various combinations thereof.

[0082] In some instances the vaccines of the invention may comprise several antigens, fragments or variants encoded by essential genes identified according to the invention. Alternatively, the vaccine may further comprise antigens identified by other methods, or specific to other bacteria, e.g., in order to provide multivalent vaccines.

[0083] With respect to libraries according to the invention, a library of polynucleotides or a library of transposon insertion sites is a collection of sequence information, which information is provided in either biochemical form (e.g., as a collection of polynucleotide molecules), or in electronic form (e.g., as a collection of polynucleotide sequences stored in a computer-readable form, as in a computer system and/or as part of a computer program). The sequence information of the polynucleotides can be used in a variety of ways, for instance as a resource for gene discovery, i.e., for identifying and verifying essential and important genes in P. aeruginosa, or for identifying essential or important homologues in other genera or species. A polynucleotide sequence in a library can be a polynucleotide that represents an mRNA, polypeptide, or other gene product encoded by the polynucleotide, and accordingly such a polynucleotide library could be used to formulate corresponding RNA or amino acid libraries according to the sequences of the library members.

[0084] The nucleotide sequence information of the library can be embodied in any suitable form, e.g., electronic or biochemical forms. For example, a library of sequence information embodied in electronic form comprises an accessible computer data file (or, in biochemical form, a collection of nucleic acid molecules) that contains the representative nucleotide sequences of essential and important genes and/or insertion mutants that are differentially expressed (e.g., attenuated growth mutants). Other combinations and comparisons of cells affected by various diseases or stages of disease will be readily apparent to the ordinarily skilled artisan. Biochemical embodiments of the library include a collection of nucleic acids that have the sequences of the genes or

transposon insertion sites in the library, where the nucleic acids can correspond to the entire gene in the library or to a fragment thereof, as described in greater detail below.

[0085] The polynucleotide libraries of the subject invention generally comprise sequence information of a plurality of polynucleotide sequences, where at least one of the polynucleotides has a sequence of any of the sequences in Tables 1-3. By plurality is meant at least 2, usually at least 3 and can include up to all of the sequences included in these tables. The length and number of polynucleotides in the library will vary with the nature of the library, e.g., if the library is an oligonucleotide array, a cDNA array, a computer database of the sequence information, etc.

[0086] Where the library is an electronic library, the nucleic acid sequence information can be present in a variety of media. "Media" refers to a manufacture, other than an isolated nucleic acid molecule, that contains the sequence information of the present invention. Such a manufacture provides the genome sequence or a subset thereof in a form that can be examined by means not directly applicable to the sequence as it exists in a nucleic acid. For example, the nucleotide sequence of the present invention, e.g. the nucleic acid sequences of any of the polynucleotides of Tables 1-3, can be recorded on computer readable media, e.g. any medium that can be read and accessed directly by a computer. Such media include, but are not limited to: magnetic storage media, such as a floppy disc, a hard disc storage medium, and a magnetic tape; optical storage media such as CD-ROM; electrical storage media such as RAM and ROM; and hybrids of these categories such as magnetic/optical storage media. One of skill in the art can readily appreciate how any of the presently known computer readable mediums can be used to create a manufacture comprising a recording of the present sequence information. "Recorded" refers to a process for storing information on computer readable medium, using any such methods as known in the art. Any convenient data storage structure can be chosen, based on the means used to access the stored information. A variety of data processor programs and formats can be used for storage, e.g. word processing text file, database format, etc. In addition to the sequence information, electronic versions of the libraries of the invention can be provided in conjunction or connection with other computer-readable information and/or other types

of computer-readable files (e.g., searchable files, executable files, etc, including, but not87 limited to, for example, search program software, etc.).

[0087] By providing the nucleotide sequence in computer readable form, the information can be accessed for a variety of purposes. Computer software to access sequence information is publicly available. For example, the gapped BLAST (Altschul et al. Nucleic Acids Res. (1997) 25:3389-3402) and BLAZE (Brutlag et al. Comp. Chem. (1993) 17:203) search algorithms on a Sybase system can be used to identify open reading frames (ORFs) within the genome that contain homology to ORFs from other organisms.

[0088] As used herein, "a computer-based system" refers to the hardware means, software means, and data storage means used to analyze the nucleotide sequence information of the present invention. The minimum hardware of the computer-based systems of the present invention comprises a central processing unit (CPU), input means, output means, and data storage means. A skilled artisan can readily appreciate that any one of the currently available computer-based system are suitable for use in the present invention. The data storage means can comprise any manufacture comprising a recording of the present sequence information as described above, or a memory access means that can access such a manufacture.

[0089] "Search means" refers to one or more programs implemented on the computer-based system, to compare a target sequence or target structural motif, or expression levels of a polynucleotide in a sample, with the stored sequence information. Search means can be used to identify fragments or regions of the genome that match a particular target sequence or target motif. A variety of known algorithms are publicly known and commercially available, e.g. MacPattern (EMBL), BLASTN and BLASTX (NCBI). A "target sequence" can be any polynucleotide or amino acid sequence of six or more contiguous nucleotides or two or more amino acids, preferably from about 10 to 100 amino acids or from about 30 to 300 nucleotides. A variety of comparing means can be used to accomplish comparison of sequence information from a sample (e.g., to analyze target sequences, target motifs, or relative expression levels) with the data storage means. A skilled artisan can readily recognize that any one of the publicly

available homology search programs can be used as the search means for the computer based systems of the present invention to accomplish comparison of target sequences and motifs. Computer programs to analyze expression levels in a sample and in controls are also known in the art.

[0090] A "target structural motif," or "target motif," refers to any rationally selected sequence or combination of sequences in which the sequence(s) are chosen based on a three-dimensional configuration that is formed upon the folding of the target motif, or on consensus sequences of regulatory or active sites. There are a variety of target motifs known in the art. Protein target motifs include, but are not limited to, enzyme active sites and signal sequences. Nucleic acid target motifs include, but are not limited to, hairpin structures, promoter sequences and other expression elements such as binding sites for transcription factors.

[0091] The present invention encompasses the use of the library of essential and important genes to search for polynucleotide and amino acid sequences in common among the essential and important genes. Such identified sequences can be used to design and develop antibacterial agents and vaccines against *Pseudomonas aeruginosa*.

[0092] A variety of structural formats for the input and output means can be used to input and output the information in the computer-based systems of the present invention. One format for an output means ranks the relative expression levels of different polynucleotides. Such presentation provides a skilled artisan with a ranking of relative expression levels to determine a gene expression profile.

[0093] As discussed above, the "library" as used herein also encompasses biochemical libraries of the polynucleotides of Tables 1-3, e.g., collections of nucleic acids representing the provided polynucleotides. The biochemical libraries can take a variety of forms, e.g., a solution of cDNAs, a pattern of probe nucleic acids stably associated with a surface of a solid support (i.e., an array) and the like. Of particular interest are nucleic acid arrays in which one or more of the sequences of Tables 1-3 is represented on the array. By "array" is meant a an article of manufacture that has at least a substrate with at least two distinct nucleic acid targets on one of its surfaces, where the number of distinct nucleic acids can be considerably higher, typically being

at least 10 nt, usually at least 20 nt and often at least 25 nt. A variety of different array formats have been developed and are known to those of skill in the art. The arrays of the subject invention find use in a variety of applications, including gene expression analysis, drug screening, mutation analysis and the like, as disclosed in the above-listed exemplary patent documents.

[0094] In addition to the above nucleic acid libraries, analogous libraries of polypeptides are also provided, where the polypeptides of the library will represent at least a portion of the polypeptides encoded by a gene corresponding to one or more of the sequences in Tables 1-3.

[0095] "Identity" as it is used in the present invention should be distinguished from "homology" or "homologous." In the context of the coding sequences and genes of this invention, "homologous" refers to genes whose expression results in expression products which have a combination of amino acid sequence similarity (or base sequence similarity for transcript products) and functional equivalence, and are therefore homologous genes. In general such genes also have a high level of DNA sequence similarity (i.e., greater than 80% identity when such sequences are identified among members of the same genus, but lower when these similarities are noted across bacterial genera), but are not identical. Relationships across bacterial genera between homologous genes are more easily identified at the polypeptide (i.e., the gene product) rather than the DNA level. The combination of functional equivalence and sequence similarity means that if one gene is useful, e.g., as a target for an antibacterial agent, or for screening for such agents, then the homologous gene is probably also useful, but may not react in the same manner or to the same degree to the activity of a specific antibacterial agent.

[0096] Nevertheless, the identification of one such gene serves to identify a homologous gene through the same relationships as indicated above, and can serve as a starting point to determine whether the homologous gene is also essential, whether it responds to the same antibacterial agents, etc. Typically, such homologous genes are found in other bacterial species, especially, but not restricted to, closely related species. Due to the DNA sequence similarity, homologous genes are often identified by

hybridizing with probes from the initially identified gene under hybridizing conditions that allow stable binding under appropriately stringent conditions. For instance, nucleic acids having sequence similarity are detected by hybridization under low stringency conditions, for example, at 50°C and 10XSSC (0.9 M saline/0.09 M sodium citrate) and remain bound when subjected to washing at 55°C in 1XSSC. Sequence identity can be determined by hybridization under stringent conditions, for example, at 50°C or higher and 0.1XSSC (9 mM saline/0.9 mM sodium citrate). Hybridization methods and conditions are well known in the art, see, e.g., USPN 5,707,829. Nucleic acids that are substantially identical to the provided polynucleotide sequences, e.g. allelic variants, genetically altered versions of the gene, etc., bind to the provided polynucleotide sequences under stringent hybridization conditions. By using probes, particularly labeled probes of DNA sequences, one can isolate homologous or related or substantially identical genes. The equivalent function of the product is then verified using appropriate biological and/or biochemical assays.

[0097] Using such hybridization technique for the identification of homologous genes, it will be possible to screen other species of bacteria, particularly other genera of gram negative pathogenic bacteria although gram positive bacteria may also be screened, to determine if any essential or important gene identified herein has a homologue in that particular genus of bacteria. If so, such gene could be cloned and isolated for essentiality in the particular genus, and further tested for sensitivity or susceptibility to the antibacterial agents and inhibitors identified herein. Specific genera of bacteria particularly appropriate for hybridization screening for the presence of homologues of essential and important genes include Escherichia, Hemophilus, Vibrio, Borrelia, Enterococcus, Heliobacter, Legionella, Mycobacterium, Mycoplasma, Neisseria, Staphylococcus, Streptococcus, etc.

[0098] "Identity," on the other hand, is gauged from the starting point of complete homology. Thereafter, identity may be described in terms of percentages according to the number of base changes in the DNA sequence taking into account any gaps. For purposes of the present invention, variants of the invention have a sequence identity greater than at least about 65%, preferably at least about 75%, more preferably at least about 85%, and can be greater than at least about 90% or more as determined by the

Smith-Waterman homology search algorithm as implemented in MPSRCH program (Oxford Molecular). A preferred method of calculating percent identity is the Smith-Waterman algorithm, using the following. Global DNA sequence identity must be greater than 65% as determined by the Smith-Waterman homology search algorithm as implemented in MPSRCH program (Oxford Molecular) using an affine gap search with the following search parameters: gap open penalty, 12; and gap extension penalty, 1.

[0099] Amino acid sequence variants are also included in the invention. Preferably, naturally or non-naturally occurring protein variants have amino acid sequences which are at least 85%, 90%, or 95% identical to the amino acid sequences identified herein, or to a shorter portion of these sequences. More preferably, the molecules are 98% or 99% identical. Percent sequence identity is determined using the Smith-Waterman homology search algorithm using an affine gap search with a gap open penalty of 12 and a gap extension penalty of 2, BLOSUM matrix of 62. The Smith-Waterman homology search algorithm is taught in Smith and Waterman, Adv. Appl. Math. (1981) 2:482-489.

[0100] Also included in the invention are fragments of the nucleic acid sequences and amino acid sequences identified herein, as well as RNAs and RNA fragments corresponding to the DNA sequences disclosed. Such nucleic acid fragments are at least about 10 nucleotides, more preferably at least about 20 to 25 nucleotides, and more preferably at least about 50 to 100 nucleotides, and can include any fragment or variant of a fragment. Such nucleic acid fragments may be used as probes for identifying similar or substantially identical or identical nucleic acid sequences in other genera, or as tools in constructing nucleic acid vectors for knock out and promoter swap experiments. Such amino acid fragments are at least about four amino acids in length, more preferably at least about 8 to 12 amino acids in length, and more preferably at least about 20 to 30 amino acids in length, and may be used as agonists or antagonists to test binding interactions of the proteins disclosed herein, or alternatively as immunogens to isolate antibodies that recognize and bind to specific epitopes of a target protein.

[0101] Once a gene is identified as being essential or important for *Pseudomonas* growth on rich media or in any specific environment, the invention also encompasses the identification of antibacterial agents that have specific activity against the essential or important genes or their gene products or the biochemical pathways in which they are involved. In this context, the term "biochemical pathway" refers to a connected series of biochemical reactions normally occurring in a cell, or more broadly a cellular event such as cellular division or DNA replication. Typically, the steps in such a biochemical pathway act in a coordinated fashion to produce a specific product or products or to produce some other particular biochemical action. Such a biochemical pathway requires the expression product of a gene if the absence of that expression product either directly or indirectly prevents the completion of one or more steps in that pathway, thereby preventing or significantly reducing the production of one or more normal products or effects of that pathway.

[0102] Thus, an agent specifically inhibits such a biochemical pathway requiring the expression product of a particular gene if the presence of the agent stops or substantially reduces the completion of the series of steps in that pathway. Such an agent, may, but does not necessarily, act directly on the expression product of that particular gene. An "expression product" of a gene means that, in a bacterial cell of interest, the gene is transcribed to form RNA molecules. For those genes that are transcribed into mRNAs, the mRNA is translated to form polypeptides. More generally, in this context, "expressed" means that a gene product is formed at the biological level that would normally have the relevant biological activity (i.e., RNA or polypeptide level).

[0103] Thus, the invention includes a method of screening for an antibacterial agent, comprising determining whether a test compound is active against an essential or important bacterial gene identified by the methods herein. The invention also includes a method of screening for an antibacterial agent, comprising determining whether a test compound is active against a protein encoded by an essential bacterial gene identified herein, or active to inhibit the biochemical pathway that involves said protein. The term "antibacterial agent" refers to both naturally occurring antibiotics produced by microorganisms to suppress the growth of other microorganisms, and agents

synthesized or modified in the laboratory which have either bactericidal or bacteriostatic activity. An "active" agent in this context will inhibit the growth of *P. aeruginosa* and possibly related species. The term "inhibiting the growth" indicates that the rate of increase in the numbers of a population of a particular bacterium is reduced. Thus, the term includes situations in which the bacterial population increases but at a reduced rate, as well as situations where the growth of the population is stopped, as well as situations where the numbers of the bacteria in the population are reduced or the population even eliminated. If an enzyme activity assay is used to screen for inhibitors, one can make modifications in uptake/efflux, solubility, half life, etc. to compounds in order to correlate enzyme inhibition with growth inhibition.

[0104] Assays may include any suitable method and may be expected to vary on the type of essential gene or protein involved. For instance, one embodiment is a method comprising the steps of:

- a) contacting said protein or a biologically active fragment thereof with a test compound; and
- b) determining whether said test compound binds to said essential gene product or protein or fragment of said protein; wherein binding of said test compound to said polypeptide or said fragment is

wherein binding of said test compound to said polypeptide or said fragment is indicative that said test compound is an antibacterial agent. It is quite common in identifying antibacterial agents, to assay for binding of a compound to a particular polypeptide where binding is an indication of a compound which is active to modulate the activity of the polypeptide. Binding may be determined by any means according to the agent tested and techniques known in the art.

[0105] Also, agents that inhibit binding of two proteins or polypeptides may also be identified, for instance using a yeast two-hybrid system. Such a system will entail cloning the genes encoding each protein and expressing each in a reporter cell system such that interaction between the two proteins is monitored by observing the expression of a reporter gene. For instance, cDNAs cloned in a yeast two-hybrid expression system (Chien et al. (1991) Proc. Natl. Acad. Sci. (U.S.A.) 88: 9578; Zervos et al. (1993) Cell 72: 233) can be used to identify other cDNAs encoding proteins that

interact with the protein encoded by the first, thereby produce expression of the GAL4-dependent reporter gene. Thereafter, cells expressing both proteins leading to expression of the reporter gene are used to screen for agents that interact with either protein, or the gene encoding either protein. Such systems are well known in the art and are well within the realm of ordinary skill.

- [0106] Another embodiment is a method for evaluating a test agent for inhibition of expression of an essential gene identified according to the methods herein, comprising:
 - a) contacting a cell expressing said essential gene with said agent; and
 - b) determining the amount or level of expression of said essential gene in said sample.
- [0107] The exact determination method will be expected to vary depending on the characteristics of the expression product as would be readily apparent to one of ordinary skill in the art. Such methods can include, for example, antibody binding methods, enzymatic activity determinations, and substrate analog binding assays. Such level of expression could be monitored by monitoring the level of the product of the essential gene in the cell, i.e., by SDS-PAGE, or by colorimetric assays using, for example, a *lacZ* gene or protein fusion and detection on media using X-Gal or spectrophotometric detection.
- [0108] When such fusions are employed, fusions may be designed using the chromosomal gene so long as the fusion does not disrupt the function of the essential gene, i.e., as with a gene fusion where lacZ is inserted just downstream of the essential gene and is expressed from the same promoter as the essential gene. Alternatively, one could employ an extrachromosomal fusion construct whereby the wild type chromosomal copy of the gene is not disrupted. In this case, one could employ a protein fusion, i.e., where a portion of lacZ sufficient to be detected with a colorimetric test is fused in frame with the coding region of the essential gene such that a fusion protein is obtained. Other detectable or measurable proteins commonly used in the art may be used as an alternative to lacZ, for instance, phoA, Lux/luciferase, etc.
- [0109] Another method of the invention for evaluating an potential antibacterial agent, comprises the steps of:

- a) providing a bacterial strain comprising a mutant or normal form of the essential or important gene, wherein said mutant form of the gene confers a growth conditional phenotype;
- b) contacting bacteria of said bacterial strain with a test compound in semipermissive or permissive growth conditions; and
- c) determining whether the growth of said bacterial strain comprising said mutant form of a gene is reduced in the presence of said test compound to a greater extent than a comparison bacteria comprising a normal form of said gene.

[0110] In this context, a "mutant form" of a gene is a gene which has been altered, either naturally or artificially, changing the base sequence of the gene, which results in a change in the amino acid sequence of an encoded polypeptide. The change in the base sequence may be of several different types, including changes of one or more bases for different bases, small deletions, and small insertions. Mutations may also include transposon insertions that lead to attenuated activity, i.e., by resulting in expression of a truncated protein. By contrast, a normal form of a gene is a form commonly found in a natural population of a bacterial strain. Commonly a single form of a gene will predominate in natural populations. In general, such a gene is suitable as a normal form of a gene, however, other forms which provide similar functional characteristics may also be used as a normal gene. In particular, a normal form of a gene does not confer a growth conditional phenotype on the bacterial strain having that gene, while a mutant form of a gene suitable for use in these methods does provide such a growth conditional phenotype.

[0111] As used in the present disclosure, the term "growth conditional phenotype" indicates that a bacterial strain having such a phenotype exhibits a significantly greater difference in growth rates in response to a change in one or more of the culture parameters than an otherwise similar strain not having a growth conditional phenotype. Typically, a growth conditional phenotype is described with respect to a single growth culture parameter, such as temperature. Thus, a temperature (or heat-sensitive) mutant (i.e., a bacterial strain having a heat-sensitive phenotype) exhibits significantly reduced growth, and preferably no growth, under non-permissive temperature conditions as

compared to growth under permissive conditions. In addition, such mutants preferably also show intermediate growth rates at intermediate, or semi-permissive, temperatures. Similar responses also result from the appropriate growth changes for other types of growth conditional phenotypes. A growth conditional phenotype can also be conferred by cloning an essential or important gene behind a regulatable promoter, for instance, a promoter that is only active, or only leads to transcription, under particular environmental conditions or in response to a specific environmental stimulus. Such growth conditional promoter mutants may be isolated according to the promoter swap strategies described herein.

[0112] "Semi-permissive conditions" are conditions in which the relevant culture parameter for a particular growth conditional phenotype is intermediate between permissive conditions and non-permissive conditions. Consequently, in semi-permissive conditions the bacteria having a growth conditional phenotype will exhibit growth rates intermediate between those shown in permissive conditions and non-permissive conditions. In general, such intermediate growth rate is due to a mutant cellular component which is partially functional under semi-permissive conditions, essentially fully functional under permissive conditions, and is non-functional or has very low function under non-permissive conditions, where the level of function of that component is related to the growth rate of the bacteria.

[0113] The term "method of screening" means that the method is suitable, and is typically used, for testing for a particular property or effect in a large number of compounds. Therefore, the method requires only a small amount of time for each compound tested; typically more than one compound may be tested simultaneously (as in a 96-well microtiter plate, or in a series of replica plates), and preferably significant portions of the procedure can be automated. "Method of screening" also refers to determining a set of different properties or effects of one compound simultaneously.

[0114] Because the essential and important genes identified herein can be readily isolated and the genes cloned into a variety of vectors known in the art, the invention also encompasses vectors comprising the nucleic acid sequences, open reading frames and genes of the invention, as well as host cells containing such vectors. Because the

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essential genes identified herein can be readily isolated and the encoded gene products expressed by routine methods, the invention also provides the polypeptides encoded by those genes, as well as genes having at least about 50%, or more preferably about 60%, or more preferably about 70%, or more preferably about 80%, or more preferably about 90%, or most preferably about 95% protein sequence identity.

[0115] Thus, by identifying certain essential and/or important genes, this invention provides a method of screening for an antibacterial agent by contacting a polypeptide encoded by one of the identified essential or important genes, or a biologically active fragment of such a polypeptide, with a test compound, and determining whether the test compound binds to the polypeptide or polypeptide fragment. In addition, to simple binding determinations, the invention provides a method for identifying or evaluating an agent active on one of the identified essential genes. The method involves contacting a sample containing an expression product of one of the identified genes with the known or potential agent, and determining the amount or level of activity of the expression product in the sample.

[0116] In particular, antibodies to essential and important gene products are anticipated to be suitable diagnostic binding and antibacterial agents. Thus, antibodies to the proteins encoded by the essential and important genes identified by the methods described herein are also included in the invention. Such antibodies may be isolated according to well known techniques in the art, i.e., Kohler and Milstein for monoclonal antibodies. Also included are polyclonal antibodies and antibody fragments such as Fv, Fab and Fab₂ fragments, as well as chimeric and humanized antibodies, and human antibodies, i.e., made using a Xeno mouse.

[0117] In a further aspect, this invention provides a method of diagnosing the presence of a bacterial strain having one of the genes identified above, by probing with an oligonucleotide at least 15 nucleotides in length, which specifically hybridizes to a nucleotide sequence which is the same as or complementary to the sequence of one of the bacterial genes identified above. In some cases, it is practical to detect the presence of a particular bacterial strain by direct hybridization of a labeled oligonucleotide to the

particular gene. In other cases, it is preferable to first amplify the gene or a portion of the gene before hybridizing labeled oligonucleotides to those amplified copies.

[0118] In a related aspect, this invention provides a method of diagnosing the presence of a bacterial strain by specifically detecting the presence of the transcriptional or translational product of the gene. Typically, a transcriptional (RNA) product is detected by hybridizing a labeled RNA or DNA probe to the transcript. Detection of a specific translational (protein) product can be performed by a variety of different tests depending on the specific protein product. Examples would be binding of the product by specific labeled antibodies and, in some cases, detection of a specific reaction involving the protein product. Diagnostic assays find particular use in assaying tissue and fluid samples of patients suspect of having a *Pseudomonas* infection.

[0119] Antibacterial agents identified according to the methods of the invention may be employed in pharmaceutical compositions. Such compositions may be administered to patients in order to treat an infection by or involving *P. aeruginosa*, either alone or in combination with secondary agents targeted at, for instance virulence factors of *P. aeruginosa*, or other bacteria that may be present in addition to *P. aeruginosa*. In this context, the term "administration" or "administering" refers to a method of giving a dosage of an antibacterial pharmaceutical composition to a mammal, where the method is, e.g., topical, oral, intranasal, inhaled, intravenous, transdermal, intraperitoneal, or intramuscular. The preferred method of administration can vary depending on various factors, e.g., the components of the pharmaceutical composition, the site of the potential or actual bacterial infection, the bacterium involved, and the severity of an actual bacterial infection.

[0120] As used above and throughout this application, "hybridize" has its usual meaning from molecular biology. It refers to the formation of a base-paired interaction between nucleotide polymers. The presence of base pairing implies that at least an appreciable fraction of the nucleotides in each of two nucleotide sequences are complementary to the other according to the usual base pairing rules. The exact fraction of the nucleotides which must be complementary in order to obtain stable

hybridization will vary with a number of factors, including nucleotide sequence, salt concentration of the solution, temperature, and pH.

[0121] The term, "DNA molecule", should be understood to refer to a linear polymer of deoxyribonucleotides, as well as to the linear polymer, base-paired with its complementary strand, forming double-strand DNA (dsDNA). The term is used as equivalent to "DNA chain" or "a DNA" or "DNA polymer" or "DNA sequence", so this description of the term meaning applies to those terms also. The term does not necessarily imply that the specified "DNA molecule" is a discrete entity with no bonding with other entities. The specified DNA molecule may have H-bonding interactions with other DNA molecules, as well as a variety of interactions with other molecules, including RNA molecules. In addition, the specified DNA molecule may be covalently linked in a longer DNA chain at one, or both ends. Any such DNA molecule can be identified in a variety of ways, including, by its particular nucleotide sequence, by its ability to base pair under stringent conditions with another DNA or RNA molecule having a specified sequence, or by a method of isolation which includes hybridization under stringent conditions with another DNA or RNA molecule having a specified sequence.

[0122] References to a "portion" of a DNA or RNA chain mean a linear chain which has a nucleotide sequence which is the same as a sequential subset of the sequence of the chain to which the portion refers. Such a subset may contain all of the sequence of the primary chain or may contain only a shorter sequence. The subset will contain at least 15 bases in a single strand. However, by "same" is meant "substantially the same"; deletions, additions, or substitutions of specific nucleotides of the sequence, or a combination of these changes, which affect a small percentage of the full sequence will still leave the sequences substantially the same. Preferably this percentage of change will be less than 20%, more preferably less than 10%, and even more preferably less than 3%. "Same" is therefore distinguished from "identical"; for identical sequences there cannot be any difference in nucleotide sequences.

[0123] As used in reference to nucleotide sequences, "complementary" has its usual meaning from molecular biology. Two nucleotide sequences or strands are

complementary if they have sequences that would allow base pairing between the strands according to the usual pairing rules. This does not require that the strands would necessarily base pair at every nucleotide; two sequences can still be complementary with a low level of base mismatch such as that created by deletion, addition, or substitution of one or a few (up to 5 in a linear chain of 25 bases) nucleotides, or a combination of such changes.

[0124] Other embodiments of the invention will be immediately envisaged by those of skill in the art upon reading the methods and examples to follow. Such examples are merely illustrative of the invention, and should not be construed as limiting the scope of the invention in any way.

Methodology

Generation of Transposon Library

[0125] Transposon insertions were generated using an improved transposon system for *P. aeruginosa* that utilizes a mini-Tn5-type transposon on a delivery vector that does not replicate in *Pseudomonas*. The delivery vector contains a modified transposase gene with three amino acid substitutions that have been shown to increase the frequency of Tn5 insertions. Weinreich et al., 1994, Evidence that cis preference of the Tn5 transposase is caused by nonproductive multimerization, Genes Dev. 8(19): 2363-74. The Tn5 transposase was placed under control of a *lac* promoter and the complete transposable element was minimized to 1.7 kilobases in length, including a tetracycline resistance marker and transcription terminator to prevent read-through into the genome. The transposon vector is delivered to *P. aeruginosa* via conjugation from a suitable *E. coli* host (e.g. SM10λ*pir*). Following conjugation, transposon mutants are selected by resistance to tetracycline conferred by the trasnposable element.

[0126] Libraries were created in both *P. aeruginosa* PAK and PA01. The average diversity of the libraries created using this strategy is estimated to be ~40,000 to ~50,000 independent mutants per conjugation. Care is taken to minimize passage of each transposon conjugation before plating for mutant selection in an effort to minimize

the potential for siblings, i.e., by stopping the conjugation after sufficient time for a single round of conjugation events.

High-Throughput Transposon Insertion Mapping (HTTIM)

[0127] Precise transposon insertion sites were determined by an anchored, semi-random PCR method for amplification of the transposase/genome junction region. O'Toole and Kolter, 1998, Initiation of biofilm formation in *Pseudomonas fluorescens* WCS365 proceeds via multiple, convergent signaling pathways: a genetic analysis, Mol. Microbiol. 28(3): 449-61. The technique, HTTIM, uses both Tn5 specific and semi-random primers with conserved primer tails. A small aliquot of transposon mutant liquid culture is used as a template and amplification of a fragment containing an insertion site is achieved in a two-step process. The PCR product is then sequenced and the insertion site is entered into an Oracle database for analysis. To date, more than 10,000 to 14,000 insertions have been mapped, each insertion representing the disruption of a gene or intergenic region that is not essential for survival on rich media.

[0128] With every insertion added to the map, the regions of the genome containing essential genes, and particularly those containing operons containing essential genes (because of potential polar effects of insertions in upstream genes), begin to become apparent because these regions will not be able to accommodate transposon insertions. Table 1 shows a listing of the open reading frames identified as existing between transposon insertions, as well as an indication of whether the gene has homologues that have been identified in other bacteria pursuant to BLAST sequence database analysis. Open reading frames were tentatively assigned names prior to being identified pursuant to HTTIM analysis, as disclosed in the *Pseudomonas* genome project, and reported in Stover et al., Complete genome sequence of *Pseudomonas aeruginosa* PAO1, an opportunistic pathogen, August 21, 2000, Nature 406: 959-964, herein incorporated by reference in its entirety.

[0128] For instance, the predicted ORFs were examined individually for (1) identity with known genes of *P. aeruginosa* with sequences deposited in GenBank, (2)

similarity with well-characterized genes from other bacteria, or (3) presence of known functional motifs (see http://www.pseudomonas.com for complete list). In each case the literature was searched to ensure that the proteins encoded by the homologous genes were functionally characterized to avoid the perpetuation of poorly supported functional assignments. In addition, 61 researchers who were members of the *P. aeruginosa* research community or had experience in particular aspects of bacterial physiology were enlisted for the *Pseudomonas* Community Annotation Project (PseudoCAP) to provide expert assistance and confirmatory information in the genome project for the analysis of identified ORFs and assigned functions.

[0129] The genome project was able to assign a functional class to 54.2% of ORFs. As in other bacterial genomes, a large proportion of the genome (45.8% of ORFs) consists of genes for which no function could be determined or proposed (confidence level 4). Of these, nearly a third (769 ORFs) possess homology to genes of unknown function predicted in other bacterial genomes, and the remainder (32% of ORFs) do not have strong homology with any reported sequence. The 372 ORFs from the entire genome analysis that are known *P. aeruginosa* genes with demonstrated functions (confidence level 1) are primarily genes encoding lipopolysaccharide biosynthetic enzymes, virulence factors, such as exoenzymes and the systems that secrete them, and proteins involved in motility and adhesion. ORFs with strong homology to genes in other organisms with demonstrated functions (confidence level 2; 1,059 ORFs) include those required for DNA replication, protein synthesis, cell-wall biosynthesis and intermediary metabolism.

[0130] The ORFs that provided the most new information about *P. aeruginosa* biology via the genome annotation were those that could be assigned a probable function on the basis of similarity to established sequence motifs, but could not be assigned a definite name (confidence level 3; 1,590 ORFs). Most of these genes encode products that are in one of three functional classes: putative enzymes (405 genes), transcriptional regulators (341 genes) or transporters of small molecules (408 genes). In some cases genomic context provided additional information, allowing us to identify loci that appear to encode systems such as metabolic pathways and secretion systems, although the substrates for such systems could not be identified. The system

for assigning name and putative function to each essential or important gene was gleaned from the *Pseudomonas* genome project data already available.

Statistical Analysis of Putative Essential and Important Genes

[0131] The open reading frames listed in Table 1 are also presented in Table 2, wherein the ORFs are listed in order of length of base pairs from longest to shortest. Also listed in Table 2 is the probability of essentiality assigned to each of the open reading frames. Probability correlates with length of the ORF, such that the longer the ORF, the higher the probability of hitting the ORF in a random transposon mutagenesis experiment, and the higher the confidence level that the ORF represents an essential or an important gene given that no transposon insertions therein were isolated. Statistical confidence levels in essentiality or importance can help narrow the focus in the screening of specific genes, thereby shortening the verification process and the subsequent identification of antibacterial agents specific for that gene or gene product. Thus, one of the benefits of the HTTIM approach is that it is a quantitative approach that lends itself well to statistical analysis.

[0132] The High-Throughput Transposon Insertion Mapping (HTTIM) strategy utilizes a transposon, which is a small, mobile DNA element that randomly inserts into the chromosome. Although HTTIM was performed using a Tn5 transposon, any transposon may be employed so long as its insertion into the chromosome is random, i.e., devoid of hot spots. Reznikoff, W.S., 1993, The Tn5 transposon, Annu. Rev. Microbiol. 47: 945-63. Although the Tn5 derivative employed here contained a modified transposase gene with three amino acid substitutions that have been shown to increase the frequency of Tn5 insertions (see supra), the frequency of insertion is generally quite low. For instance, mutants with even one insertion occur at a rate of only 1 in 10⁵ or 10⁶ bacteria, and must be specifically selected from a background of cells with no insertions. Because the frequency of a single insertion is so low, the frequency of a double insertion is so low as to be insignificant.

[0133] When the transposon insertion disrupts one of the 5570 genes in the *Pseudomonas* genome, the function of that gene is lost. If the disrupted gene is essential for growth, the transposon insertion mutant dies and cannot be characterized.

If the transposon disrupts a gene that is non-essential, the mutant survives, grows and the transposon insertion site is mapped. By examining the insertion sites of a large number of transposon mutants, all, of the non-essential *P. aeruginosa* genes can be identified, and by implication, all of the essential genes may be identified as well. Characterization of over 13,000 transposon insertions revealed insertions in 3890 genes and resulted in an even distribution of insertions across the entire length of the genome. The remaining 1658 genes, in which a transposon insertion has never been observed, are candidates of essential genes (30%). *See* Figure 7, showing a graph illustrating ORF coverage by Tn5 achieved in High-Throughput Transposon Insertion Mapping (HTTIM), wherein 30% of the genes in the genome are candidate essential genes where ORF size is not taken into account in predicting essentiality.

[0134] Because insertion of the transposon used here into the chromosome was proposed to be random, it was possible that some of the 1658 genes that did not receive a transposon insertion were simply not hit by random chance. One cannot truly know that a transposon has no hot spots and is entirely random until the data is analyzed, and the data here confirmed that the Tn5 derivative employed underwent random insertion in P. aeruginosa. Thus, the chance that a gene will not be hit by the transposon as a matter of random chance increases as the length of the gene decreases, particularly for very small genes (< 600 base pairs). See Figure 8, Probability of Being an Essential Gene Given No Hit. Thus, by deleting smaller ORFs (< 600 base pairs) in which there is a lower confidence in essentiality, the probability of essentiality goes up while the number of predicted essential genes decreases. Further, the curve in the graph depicted in Figure 8 should level off faster. Thus, in predicting the essentiality of genes from the HTTIM candidate set, the closer one can come to a probability of 1.0 as depicted in Figure 8, the higher the confidence level of essentiality that can be assigned to each gene in the candidate subset. For a representation of the number of ORFs of various lengths in P. aeruginosa, see the histogram in Figure 9.

[0135] A Bayessian statistical model for truncated counting data was applied to the candidate essential gene set, and permitted a determination that 16 to 17 percent of *P. aeruginosa* genes are essential. Such a model may therefore be utilized to increase the

statistical confidence that a given gene in the candidate subset is essential. An exemplary statistical model is provided in Example 1.

Physical Methods for Target Gene Validation

[0136] While the above methodology and the database of putative essential and important gene candidates established thereby is believed to be superior to existing methods with regard to the quantity of experimentation required to identify essential and important genes in *Pseudomonas aeruginosa* and the degree of confidence conferred, it should be understood that the methodology described herein can be incorporated into combined protocols with technology known in the art. For instance, the methods for verifying essentiality disclose in WO 01/07651, herein incorporated by reference in its entirety, would be useful as a secondary method to be utilized in combination with the methods described in this disclosure. Alternatively or additionally, one of several approaches may be used to determine whether a particular gene is essential (absolutely required for survival on rich medium) or important (the absence of which results in attenuated growth) to *P. aeruginosa*.

Integration Knockouts

[0137] This is the simplest and most rapid strategy. PCR is used to amplify a small (200-500 base pairs) portion of the coding sequence, or open reading frame (ORF) of the gene of interest. This gene fragment must be centrally located within the ORF--it cannot include either termini of the gene's coding region. This fragment is cloned into a plasmid vector that can replicate in *E. coli*, but not in *Pseudomonas*. The vector used should have a drug resistance marker that is suitable for selection in *Pseudomonas*, and an origin for conjugal transfer. This feature allows the plasmid to be transferred by conjugation from a suitable *E. coli* donor strain to a *Pseudomonas* strain when the two are co-cultured under the appropriate conditions.

[0138] Following conjugation the co-cultured mixture is harvested and plated on media which selects against the *E. coli* donor and for *Pseudomonas* which contain the plasmid. Since the plasmid is incapable of extra-chromosomal replication in *Pseudomonas*, colonies that arise are the result of homologous recombination between the *Pseudomonas* chromosome and the cloned gene fragment on the plasmid. This is referred to as single-crossover recombination; a single recombination event takes place between the plasmid and the chromosome. The result is integration of the plasmid into the bacterial chromosome and disruption of the gene from which the fragment was amplified (Fig. 1).

[0139] Variations of this approach are possible. For instance, one could clone out the entire locus and isolate transposon insertion mutants in *E.coli* using known techniques, i.e., by transposition from the *E. coli* genome, selecting plasmid insertions by mobilizing the vector into a recipient cell that does not contain the transposon or the antibiotic resistance marker encoded by the transposon, and screening the plasmid for insertions in the cloned gene. Thereafter, a similar assay could be performed by screening for double crossover events in *P. aeruginosa* that result in recombination of the transposon into the chromosomal locus from a suicide vector.

[0140] Integration of the plasmid or other insertion at the locus can be confirmed by a relatively rapid PCR-based screen of recombinant colonies. The advantage of this strategy, particularly the plasmid single crossover strategy, is that it requires only amplification of a short stretch of DNA followed by a single cloning step before recombination experiments can be performed. The disadvantage is that if the target gene is essential, no recombinants can be obtained. Failure to obtain recombinants as proof of essentiality is pretty thin evidence. However, if a gene is in fact non-essential, this method will demonstrate that quickly.

Integration Knockouts with Extra-chromosomal Complementation

[0141] This variation of the above method provides more convincing data when the target gene is essential. It employs the same type of non-replicating integration plasmid described above, but recombinations are performed in strains already carrying a second copy of the target gene on an extra-chromosomal plasmid. This second copy can then supply the essential function when the chromosomal copy is disrupted. If disruptions can only be obtained when a complementing plasmid is present and not when a control plasmid is present, this is rather strong evidence that the target gene is essential. The advantage of this method is that you obtain colonies even when your gene is essential. The disadvantage is that construction and sequencing of the complementation plasmid takes additional time.

Integration with a Regulatable Promoter (Promoter Swap)

[0142] This approach also involves selecting for chromosomal integration of nonreplicating plasmids via homologous recombination. However, the design of the integrating plasmid is different. In this case, the N-terminal coding sequence (300-500 base pairs) of the target gene is PCR amplified and cloned into a vector downstream of a regulatable promoter, i.e., a lac promoter, which is inducible in the presence of IPTG, or an arabinose promoter (pABD), inducible in the presence of arabinose. The activity of the promoter can be modulated by the presence of a specific inducer molecule. The plasmid is conjugated into Pseudomonas and integration selected for under conditions where the regulatable promoter is active. The resulting chromosomal integration replaces the target gene's natural promoter with the regulatable promoter from the plasmid (Fig. 2). If the target gene is essential, recombinants can only survive when the inducer molecule is present in their growth media to stimulate gene expression. If the gene is non-essential, the recombinant's growth is independent of the addition of the inducer. The advantage of this strategy is that it requires only amplification of a short stretch of DNA followed by a single cloning step before recombination experiments can be performed.

Examples: Essential Genes Identified

Example 1: A Bayessian Statistical Model for Increasing Statistical Confidence of Essentiality

[0143] When the Tn5 transposon inserts into the *Pseudomonas* DNA, one of three things happen: 1) The insertion disrupts a nonessential gene. The cell survives to be characterized and the location of the insertion is determined. 2) The insertion disrupts an essential gene. The cell does not survive and the insertion site is not determined. 3) The insertion is in an intergenic region (between genes) and no information is gained. Genes with identified insertions are nonessential genes. However, genes without identified insertions could be essential genes or nonessential genes with zero transposon insertion. To determine the number of essential genes, we have developed a multivariate Bayession model for truncated Poisson data and applied it to the *Pseudomonas* genome data set. A likelihood gain based searching algorithm was developed to obtain maximum likelihood estimates. The property of the algorithm was studied. Different approaches were compared for both multivariate and univariate approaches.

A. Structure of the Data and Preliminary Considerations

[0144] A transposon Tn5 insertion mutagenesis library was constructed in *Pseudomonas aeruginosa* strains PAK and PAO1. Mutants were randomly picked and their genomic insertion site sequence determined through polymerase chain reaction (PCR) and automated DNA sequencing. BLASTN analysis of transposon/genome junction sequences was used to map the location of the insertions relative to the completed strain PAO1 genome sequence. More than 20,000 mutants were analyzed which resulted in 12,219 independent insertions being mapped. In order to identify essential genes, transposon insertion sites were analyzed with respect to the protein-encoding genes in this organism. A data set consists of the ID of genes, their length in DNA base-pairs, and the number of transposon insertions were obtained from

experiments. The data set consists of 5570 genes with 881 different sizes ranging from 72 to 16884 DNA base-pairs. The distribution of the gene sizes are extremely skewed to the right with majority of the genes being smaller than 2000 DNA base-pairs as shown in Figure 10.

[0145] A randomly selected subset of the data is shown in Table 4, where δ is gene size, x is the observed number of transposon insertions. Insertions to essential genes are not observable since the insertion mutants can not survive for characterization when the transposon is inserted into an essential gene. Therefore, a gene with zero observed transposon insertions can either be an essential gene or a nonessential gene with zero transposon insertion. Consequently, the count of transposon insertions x is truncated with the truncation region being a single element $\{0\}$.

Table 4: A sample of the gene data set

Gene id	δ	x
298	1359	3
4047	618	0
1170	735	1
4953	1044	1
5526	213	0
4624	1707	4
5069	426	3

[0146] Since the insertion into the chromosome of *Pseudomonas aeruginosa* is random (Reznikoff WS. 1993), and the probability of receiving an insertion for a given gene is proportional to its size measured in DNA base-pairs, the number of transposon insertions into a gene is distributed as truncated Poisson with parameter $\lambda\delta$, where δ is the size of the gene and λ is an unknown parameter, which is independent of gene size.

B. <u>A Bayessian Model</u>

[0147] Let R be a measurable subset of the probability space Ω such that a random variable X is observable only if $X \in \Omega \setminus \mathbb{R}$. In this example, no observations can be obtained from essential genes, whereas only nonzero observations can be obtained from nonessential genes, the set R consists of a single element $\{0\}$.

1.

a. One Gene Size

[0148] Assume all genes in a genome have same size, δ , and let N be the number of nonessential genes in this genome. Then the observations $X_1, X_2, ..., X_N$ from the N nonessential genes are i.i.d. Poisson($\lambda \cdot \delta$), of which, all observations of value zero are truncated. The product $\lambda \cdot \delta$ indicates that the probability of a gene receiving an insertion is proportional to its size.

[0149] Let $\{X_1^*, X_2^*, \dots, X_n^*\} \subseteq \{X_1, X_2, \dots, X_N\}$ denote the subset of all nonzero observations. Then this subset composes a random sample of size n from a truncated Poisson distribution whose distribution function can be written as

$$f(x,\lambda\cdot\delta) = e^{-\lambda\cdot\delta} \frac{(\lambda\cdot\delta)^x}{x!} / (1-e^{-\lambda\cdot\delta}), \quad x = 1,2,\dots$$
 (3.1)

[0150] Let $q=1-e^{-\lambda\delta}$ denote the probability that an observation from Poisson($\lambda\cdot\delta$) is not truncated, and let $p=1-q=e^{-\lambda\delta}$. Then, conditional on the parameters n and N, the likelihood function of the joint distribution of $\{X_1^*, X_2^*, \dots, X_n^*\}$ can be written as

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$$L(\lambda \mid n, N) = (\lambda \cdot \delta)_{i=1}^{n \sum_{j=1}^{n} X_{i}^{*}} \left(\frac{p}{q}\right)^{n} \left(\prod_{i=1}^{n} X_{i}^{*}!\right)^{-1}.$$
 (3.2)

[0151] Let
$$S = X_1^* + X_2^* + \dots + X_n^*$$
 (3.3)

denote the sum of all nonzero observations and notice that n follows a binomial distribution B(N, q). The likelihood function of the joint distribution of $\{n, X_1^*, X_2^*, \dots, X_n^*\}$, conditional on the parameter N, can be obtained as

$$L(\lambda \mid N) = {N \choose n} q^n p^{N-n} (\lambda \cdot \delta)^s \left(\frac{p}{q}\right)^n \left(\prod_{i=1}^n X_i^*!\right)^{-1}$$

$$\propto {N \choose n} \lambda^s e^{-(\lambda \delta)N}.$$
(3.4)

[0152] The Bayesian model consists of the conditional model (2.4) and a prior distribution of the parameter N. Assuming N, the number of nonessential genes, is binomial B(M, γ), where M is the total number of genes of size δ , which is known, and γ is the portion of nonessential genes which is unknown and is independent of gene size, we can write the likelihood function of the joint distribution of $\{n, N, X_1^*, X_2^*, \dots, X_n^*\}$ as

$$L(\gamma,\lambda,N) \propto \binom{M}{N} \binom{N}{n} \gamma^{N} (1-\gamma)^{M-N} \lambda^{S} e^{-(\lambda \cdot S)N}. \tag{3.5}$$

[0153] This is the likelihood function of n nonzero observations from M genes of the same size δ , of which N genes are nonessential. It is easy to see that (3.5) is proportional to the likelihood function of the posterior distribution of N given observations n and S.

2.

b. Multiple Gene Sizes

[0154] For a given genome consists of genes of different sizes, let $\vec{\delta} = (\delta_1, \delta_2, \dots, \delta_g)^T$ denote the vector of g different gene sizes, and let $\vec{M} = (M_1, M_2, \dots, M_g)^T$ the vector of known numbers of total genes, $\vec{N} = (N_1, N_2, \dots, N_g)^T$ the unknown numbers of nonessential genes, $\vec{n} = (n_1, n_2, \dots, n_g)^T$ the numbers of nonzero observations from the nonessential genes, and $\vec{S} = (S_1, S_2, \dots, S_g)^T$ the sums of nonzero observations, as defined in (3.3).

[0155] The likelihood function of the joint distribution of $\{\vec{n}, \vec{N}, \vec{S}\}$ can be written as

$$L(\gamma,\lambda,\vec{N}) \propto \gamma^{\|\vec{N}\|} (1-\gamma)^{\|\vec{M}\|-\|\vec{N}\|} \lambda^{\|\vec{S}\|} e^{-\lambda (\vec{\delta}^T \cdot \vec{N})} \prod_{i=1}^{s} \binom{M_i}{N_i} \binom{N_i}{n_i} (3.6)$$

where $\|*\|$ is the L₁ norm of a vector, and $\vec{\delta}^T \cdot \vec{N} = \sum_{i=1}^g \delta_i \cdot N_i$.

[0156] Let $\Im = \ln(L)$. Then up to an additive constant, the log likelihood function of the joint distribution of $\{\vec{n}, \vec{N}, \vec{S}\}$ can be written as

$$\Im(\gamma,\lambda,\vec{N}) = ||\vec{N}|| \cdot \ln(\gamma) + (||\vec{M}|| - ||\vec{N}||) \cdot \ln(1-\gamma) + ||\vec{S}|| \cdot \ln(\lambda) - \lambda \cdot (\vec{\delta}^T \cdot \vec{N}) - \sum_{i=1}^g \ln((M_i - N_i)!) - \sum_{i=1}^g \ln((N_i - n_i)!),$$
(3.7)

where $(\gamma, \lambda, \vec{N})$ are the parameters of interests. The vector \vec{N} is defined on $\{n_i \leq N_i \leq M_i : i = 1, 2, \dots, g\}$ and $\Im(\gamma, \lambda, \vec{N})$ is proportional to the likelihood function of the posterior distribution of \vec{N} given \vec{n} and \vec{S} .

[0157] When g is large, say, in the order of hundreds as in the situation we are dealing with in this paper, obtaining the maximum likelihood (ML) estimate of $\vec{N} = (N_1, N_2, \dots, N_g)^T$ from (3.7) in such a high dimensional parameter space is a very difficult task both theoretically and computationally. In the next section, we will present a stepwise, maximum likelihood gain based method to obtain the ML estimation.

C. ML ESTIMATION OF PARAMETERS

[0158] For any $\bar{N} = (N_1, N_2, \dots, N_g)^T$, it is easy to verify using (3.7) that the ML estimations of the parameters γ and λ are

$$\hat{\gamma} = \|\vec{N}\|/\|\vec{M}\| \tag{4.1}$$

and

$$\hat{\lambda} = ||\vec{S}||/(\vec{\delta}^T \cdot \vec{N}) \tag{4.2}$$

respectively. Substituting (4.1) and (4.2) for γ and λ in (3.7), we have

$$\mathfrak{I}^{\bullet}(\vec{N}) \propto ||\vec{N}|| \cdot \ln(||\vec{N}||) + (||\vec{M}|| - ||\vec{N}||) \cdot \ln(||\vec{M}|| - ||\vec{N}||) - ||\vec{S}|| \cdot \ln(\vec{\delta}^T \cdot \vec{N}) - \sum_{i=1}^{R} (\ln((M_i - N_i)!) + \ln((N_i - n_i)!)).$$

$$(4.3)$$

[0159] For $1 \le i \le g$, define

$$\Delta_{i} \mathfrak{I}^{\bullet} \left(\vec{N} \right) = \mathfrak{I}^{\bullet} \left(\vec{N} + \vec{l}_{i} \right) - \mathfrak{I}^{\bullet} \left(\vec{N} \right) \tag{4.4}$$

for any $\vec{N} \in \{n_i \le N_i < M_i, n_j \le N_j \le M_j : i \ne j\}$. In equation (4.4), $\vec{l}_i = (0, \dots, 1, 0, \dots, 0)^T$ with 1 at the ith position. For notational purpose, let

$$\eta(k) = k \cdot \ln(k) + (\|\vec{M}\| - k) \cdot \ln(\|\vec{M}\| - k) \tag{4.5}$$

for $\|\vec{n}\| \le k < \|\vec{M}\|$. Then, (3.4) can be written as

$$\Delta_{i} \mathcal{F}^{*}(\vec{N}) = \eta \left(\|\vec{N}\| + 1 \right) - \eta \left(\|\vec{N}\| \right)$$

$$- \|\vec{S}\| \cdot \ln \left(1 + \delta_{i} / \vec{\delta}^{T} \cdot \vec{N} \right) + \ln \left(\frac{M_{i} - N_{i}}{N_{i} - n_{i} + 1} \right). \tag{4.6}$$

[0160] To obtain ML estimation of \vec{N} , we define an operator, \oplus , between the observed vector \vec{n} and any integer k with $0 \le k \le ||\vec{M}|| - ||\vec{n}||$ as follows:

$$\vec{n} \oplus 0 = \vec{n},$$

$$\vec{n} \oplus 1 = \left\{ \vec{n} + \vec{1}_i : \Delta_i \mathfrak{I}^*(\vec{n}) \ge \Delta_j \mathfrak{I}^*(\vec{n}) \text{ for all } j \ne i \right\}, \text{ and} \qquad (4.7)$$

$$\vec{n} \oplus k = \left(\vec{n} \oplus (k-1) \right) \oplus 1 \quad \text{for } k \ge 2.$$

We also define a likelihood-gain function G with G(0)=0 and

$$G(k) = \mathfrak{I}^{\bullet}(\vec{n} \oplus k) - \mathfrak{I}^{\bullet}(\vec{n} \oplus (k-1))$$
(4.8)

for $1 \le k \le ||\vec{M}|| - ||\vec{n}||$.

- [0161] Using this likelihood-gain function, we can search the ML estimation for \vec{N} as follows:
- 1. Start with the observation \vec{n} as the initial estimate of \vec{N} , and denote it as \vec{N}^0 .

- 2. For each gene size δ_i with $n_i < M_i$, i=1, 2, ..., g, calculate a likelihood difference $\Delta_i \mathfrak{I}^*(\vec{N}^0) = \mathfrak{I}^*(\vec{N}^0 + \vec{l}_i) \mathfrak{I}^*(\vec{N}^0)$ by set $N_i^0 = n_i + 1$ and $N_j^0 = n_i$ for all $j \neq i$.
- 3. Update the initial values \vec{N}^0 by setting $N_i^0 = N_i^0 + 1$ such that $\Delta_j \mathfrak{I}^*(\vec{N}^0) = \max\{\Delta_j \mathfrak{I}^*(\vec{N}^0), j = 1, 2, \dots, g\}$. This maximum likelihood difference is the likelihood gain defined in (4.8).
- 4. Repeat the process until it converges. By convergence we mean that either the estimated number of nonessential genes equals to the number of genes in each size group or when increasing the number of nonessential genes in any size groups will result in a loss of likelihood.

[0162] This algorithm searches the ML estimator in a high dimensional space (881 in our study) along a path such that at each iteration, it moves in a direction (that is, increases the number of nonessential genes in this size group by one) along which the likelihood gain is maximum among all possible directions. Because the searching algorithm prohibits reversal of previous moves at any later iteration, it moves towards the ML estimator along the shortest path with the deepest ascending (maximum likelihood gain) at each step. Table 5 and Figures 11 and 12 show the values of likelihood gains in each iteration. With very few exceptions where the monotonous is violated only at the fourth or fifth decimal places that probably can be attributed to rounding errors, the likelihood gain is a monotonously decreasing function.

Table 5. A Sample of Likelihood Gains at Each Iteration

Iteration	id	δ	M	n	$\hat{N}(i)$	G(i)
1	28	210	13	2	3	2.67559
2	60	306	14	3	4	2.41 082

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3	44	258	14	5	6	2.34388
4	63	315	15	5	6	2.29243
•••	•••	•••	•••	•••	•••	•••
18	32	222	7	1	2	2.05160
19	81	369	11	2	3	2.05166
•••	•••	•••	•••	•••	•••	•••
774	122	492	12	8	11	0.00692
775	266	924	16	14	15	0.00544
776	. 85	381	14	3	11	0.00531

The following three theorems show that the estimates obtained through the above algorithm are indeed the maximum likelihood estimates.

THEOREM 1: if

$$\sum_{i=1}^{S} \left(n_i - \exp\left(\frac{\delta_i \cdot \|\vec{S}\|}{\vec{\delta}^T \cdot \vec{n}} \right) \right) > 0, \tag{4.9}$$

then G(1)>0.

Proof: If $G(1) \le 0$, then by (4.5), $\Delta_i \mathfrak{F}(\vec{n}) \le 0$ for all $1 \le i \le g$, which leads to

$$\eta(\|\vec{n}\|+1)-\eta(\|\vec{n}\|)-\|\vec{S}\|\cdot in(1+\delta_{i}/(\vec{\delta}^{T}\cdot\vec{n}))+\ln(M_{i}-n_{i})\leq 0$$

$$\Rightarrow \|\vec{S}\| \cdot in(1+\delta_i/(\vec{\delta}^T \cdot \vec{n})) - \ln(M_i - n_i) \ge \eta(\|\vec{n}\| + 1) - \eta(\|\vec{n}\|)$$

$$\Rightarrow \frac{\left(1+\delta_{i}/\left(\vec{\delta}^{T}\cdot\vec{n}\right)\right)^{\|\vec{s}\|}}{M_{i}-n_{i}} \geq \frac{\left(\|\vec{n}\|+1\right)^{\|\vec{n}\|+1}\cdot\left(\|\vec{M}\|-\|\vec{n}\|-1\right)^{\|\vec{M}\|-\|\vec{s}\|-1}}{\left(\|\vec{n}\|\right)^{\|\vec{n}\|+1}\cdot\left(\|\vec{M}\|-\|\vec{n}\|\right)^{\|\vec{M}\|-\|\vec{s}\|}}$$

$$\Rightarrow \sum_{i=1}^{8} \left(1 + \delta_{i} / (\vec{\delta}^{T} \cdot \vec{n})\right)^{\|\vec{\delta}\|} \ge \\ \|\vec{n}\| \cdot (1 + 1/\|\vec{n}\|)^{\|\vec{n}\|+1} \cdot \left(1 + 1/(\|\vec{M}\| - \|\vec{n}\|)\right)^{\|\vec{M}\| - \|\vec{n}\|})^{\|\vec{M}\| - \|\vec{n}\|}$$

Using the facts that $(1+1/x)^x < e$, $(1+1/x)^{x+1} > e$, and $(1-1/x)^{x-1} > e^{-1}$ for any x>0, we obtain

$$\sum_{i=1}^{g} \exp \left(\frac{\delta_{i} \cdot \|\vec{S}\|}{\vec{\delta}^{T} \cdot \vec{n}} \right) \ge \|\vec{n}\| \cdot e \cdot e^{-1} = \|\vec{n}\|$$

$$\Rightarrow \sum_{i=1}^{g} \left(n_i - \exp \left(\frac{\delta_i \cdot ||\vec{S}||}{\vec{\delta}^T \cdot \vec{n}} \right) \right) < 0$$

This is contradictory to condition (4.9).

For g=1, (4.9) becomes $\ln(n) > (X_1 + X_2 + \dots + X_n)/n$. Hence, when the mean of the observed transposon insertions is less than the log of the number of nonzero observations, the vector \vec{n} can not be the ML estimator of \vec{N} and there must be truncated observations from nonessential genes.

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THEOREM 2:

$$\Delta_i \mathfrak{I}^* (\vec{N}) > \Delta_i \mathfrak{I}^* (\vec{N} - \vec{1}_j)$$
 for all $i \neq j$ (4.10)

Proof: By definition in (4.5),

$$\frac{d\left[\eta(x+1)-\eta(x)\right]}{dx} = \ln\left(\frac{x+1}{x} \cdot \frac{\|\vec{M}\|-x}{\|\vec{M}\|-x-1}\right) > 0$$

for any $0 < x < ||\vec{M}||$. Hence $\eta(||\vec{N}||+1) - \eta(||\vec{N}||)$ is an increase function of $||\vec{N}||$. Using this result, we have

$$\begin{split} &\Delta_{i}\mathcal{S}^{*}\left(\vec{N}\right) - \Delta_{i}\mathcal{S}^{*}\left(\vec{N} - \vec{1}_{j}\right) = \\ &\left(\eta\left(\parallel\vec{N}\parallel + 1\right) - \eta\left(\parallel\vec{N}\parallel\right)\right) - \left(\eta\left(\parallel\vec{N}\parallel\right) - \eta\left(\parallel\vec{N}\parallel - 1\right)\right) \\ &- \parallel\vec{S}\parallel \cdot \ln\left(1 + \delta_{i} / \left(\vec{\delta}^{T} \cdot \vec{N}\right)\right) + \parallel\vec{S}\parallel \cdot \ln\left(1 + \delta_{i} / \left(\vec{\delta}^{T} \cdot \vec{N} - \delta_{j}\right)\right) \\ &> \parallel\vec{S}\parallel \cdot \left[\ln\left(1 + \delta_{i} / \left(\vec{\delta}^{T} \cdot \vec{N} - \delta_{j}\right)\right) - \ln\left(1 + \delta_{i} / \left(\vec{\delta}^{T} \cdot \vec{N}\right)\right)\right] > 0 \end{split}$$

THEOREM 3: Under (4.9), for any $1 \le j \le g$ and $1 \le k \le K^*$,

with
$$K^* = \max\{k^* \ge 0 : G(k) \ge 0 \text{ for all } 0 \le k \le k^*\}$$
,

if
$$\vec{N} = \vec{n} \oplus k - \vec{1}_j \in \{n_j \le N_j \le M_j\}$$
, then

$$\mathfrak{I}^{\bullet}(\vec{n} \oplus k) > \mathfrak{I}^{\bullet}(\vec{n} \oplus k - \vec{1}_{j}) \tag{4.11}$$

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Proof: This is obviously true when k=1. Assume (3.11) is true for integers 1,2,..., k. For integer k+1, we have

$$\mathfrak{I}^{*}(\vec{n} \oplus (k+1) - \vec{1}_{j}) - \mathfrak{I}^{*}(\vec{n} \oplus k)$$

$$= \left[\mathfrak{I}^{*}(\vec{n} \oplus (k+1) - \vec{1}_{j}) - \mathfrak{I}^{*}(\vec{n} \oplus k - \vec{1}_{j})\right] +$$

$$\left[\mathfrak{I}^{*}(\vec{n} \oplus k - \vec{1}_{j}) - \mathfrak{I}^{*}(\vec{n} \oplus k)\right]$$

$$< \left[\mathfrak{I}^{*}(\vec{n} \oplus (k+1) - \vec{1}_{j}) - \mathfrak{I}^{*}(\vec{n} \oplus k - \vec{1}_{j})\right]$$

By theorem 2,

$$\mathfrak{I}^{\bullet}\left(\vec{n}\oplus(k+1)-\vec{1}_{j}\right)-\mathfrak{I}^{\bullet}\left(\vec{n}\oplus k-\vec{1}_{j}\right)<\mathfrak{I}^{\bullet}\left(\vec{n}\oplus(k+1)\right)-\mathfrak{I}^{\bullet}\left(\vec{n}\oplus k\right)$$

Therefore

$$\mathfrak{I}^{\bullet}(\vec{n}\oplus(k+1))>\mathfrak{I}^{\bullet}(\vec{n}\oplus(k+1)-\vec{1}_{j})$$

Combining theorems 1-3, we obtain

THEOREM 4: If the likelihood function defined in (3.7) has an unique solution, the ML estimator of \tilde{N} is:

$$\hat{\vec{N}} = \vec{n} \oplus K^* \tag{4.12}$$

[0163] Theorem 3 guarantees that the trajectory of the searching algorithm follows the shortest path in the sense that a reversal of a previous move (that is, removal of a previously added nonessential gene of any gene size) at any later state will result in a loss of likelihood. This property is illustrated in Figure 4 which shows the trajectory of the searching algorithm projected in a subspace spanned by two different gene sizes. For illustration purpose, genes are grouped into 143 groups by grouping genes with similar sizes together to increase the length of the trajectory. As indicated in the plot, at any state, moving backwards in any direction results in a loss of likelihood. Figure 13 shows more trajectories projected in different subspaces.

[0164] Now we need to demonstrate that the likelihood function (3.7), which is defined in a high dimensional discrete space, has an unique solution. This can be established if the same estimations are obtained from different initial values. Since the initial values can be any value between the observation \vec{n} and the total number of genes \vec{M} , we need to extend the searching algorithm (4.7) as follows:

For any initial value $\{\vec{N}^0: n_i \leq N_i^0 < M_i \text{ for } i=1,2,\cdots,g\}$ and any integer k with $\vec{N}^0 \oplus 0 = \vec{N}^0$, $0 \leq k \leq ||\vec{M}|| - ||\vec{N}^0||$ such that $\vec{N}^0 \oplus 1 = \{\vec{N}^0 \pm \vec{1}_i : \Delta_i \mathfrak{I}^*(\vec{N}^0) \geq \Delta_j \mathfrak{I}^*(\vec{N}^0) \text{ for all } j \neq i\}$, and (4.13) $\vec{N}^0 \oplus k = (\vec{N}^0 \oplus (k-1)) \oplus 1 \text{ for } k \geq 2.$

The likelihood gain function is extended similarly as G(0)=0 and

$$G(k) = \mathfrak{I}^{\bullet}(\vec{N}^{0} \oplus k) - \mathfrak{I}^{\bullet}(\vec{N}^{0} \oplus (k-1))$$
 (4.14)

for $1 \le k \le ||\vec{M}|| - ||\vec{N}^0||$.

[0165] Algorithm (4.13) preserves all the properties of algorithm (4.7) and it searches the ML estimator the same way as that of algorithm (4.7) with two exceptions. Unlike

algorithm (4.7), which uses \vec{n} as initial values of \vec{N} and at each iteration, the number of nonessential genes is increased by one in gene groups of size δ_i to find the maximum likelihood gain, this algorithm uses \vec{N}^0 as initial values of \vec{N} which can be greater than the ML estimator. Therefore, at each iteration, the number of nonessential genes in a group with size δ_i can be either increased or decreased by one such that the likelihood gain is maximum.

[0166] Randomly selected initial values \tilde{N}° were used for data with grouped gene sizes and data with exact gene sizes. The estimations of all parameters are exactly the same and the final likelihood for all initial values \tilde{N}° are exactly the same as indicated in Figure 14, which plots twenty seven different initial values of \tilde{N}° . The line in the far left represents the likelihood when $\tilde{N}^{\circ} = \tilde{n}$, and the lines in the middle are randomly selected. Figure 15 is the trajectory projected into a subspace spanned by two gene sizes. Each circle represents the projection of a different initial value \tilde{N}° . Regardless of the initial values, the trajectories all converge to the ML estimator.

D. ANALYSIS OF PSEUDOMONAS AERUGINOSA DATA

1. Multivariate Model with Exact Gene Sizes

[0167] The data considered here consist of observations from 5570 genes in 881 different sizes, ranging from 72 to 16884 DNA base-pairs. Distribution of gene size is severely skewed to the right as indicated in Figure 10. For many sizes, especially for sizes smaller than 200 or greater than 2000 DNA base-pairs, there is only one gene in a given size and the observation of transposon insertions for small genes are usually truncated. Since all genes are modeled simultaneously in a single model with a prior γ enforcing the essentialness of a gene being independent of its size, the sparseness of the data does not impose limitations on the computation. However, as discussed in the next section, the prior may play a dominating role for small genes where data are sparse.

The estimations of γ and λ , together with the 95 percent BCa confidence intervals are presented in Table 6 and the estimation of \vec{N} is presented in Figure 16.

Table 6. Parameter Estimation of γ and λ

	Estimate	Bias	SE	BCa Confidence Intervals		
γ	0.8434	3.942x10 ⁻³	9.893x10 ⁻³	(0.818, 0.859)		
λ	2.547x10 ⁻³	-1.027x10 ⁻⁵	4.392x10 ⁻⁵	(0.00247, 0.00264)		

Here the bias and standard error are estimated with bootstrap

2. Multivariate Model With Grouped Gene Sizes

[0168] The prior γ plays an important role in enforcing the fact that the essentialness of a gene is independent of its size. It also made possible to estimate the number of essential genes where data are very sparse. However, for small genes where data are extremely sparse, the prior γ becomes the dominating source of information. In order to moderate the dominance of the prior on small genes with sparse observations, we grouped the genes into 143 groups according to their sizes, using the median size of each group as the gene size. Table 7 is a sample of estimated \vec{N} based on grouped and exact gene sizes. In the table, m is the number of unique sizes in each group; N_1 is estimated using grouped data and N_2 is estimated using ungrouped data.

Table 7: Estimated N with Grouped and Exact Gene Sizes

Gene size	m	M	х	N	N_1	N ₂
[72, 120]	6	7	3	2	6	7
(120, 150]	4	7	3	2	6	7
(150, 160]	3	7	2	2	6	7
(160, 170]	2	8	0	0	7	7
(170, 180]	3	9	1	1	8	8
(180, 190]	3	9	1	1	8	8
(190, 200]	3	12	4	4	11	11
(200, 210]	4	27	7	7	23	24
(210, 220]	3	19	7	5	16	17
	•••	•••	•••	•••	•••	•••

[0169] We see that here $N_2 \ge N_1$. However, this is true only for data in the above table where the ungrouped data are extremely sparse and most of the data are truncated. The estimated proportion of non-essential genes, γ , is actually larger for grouped data which is presented in Table 8. Grouping genes with similar sizes reduces the sparseness of the data and consequently, the dominance of the prior. Another obvious advantage of grouping is dimension reduction of the parameter space, and therefore, drastic reduction of computation time. Of cause, such grouping introduces another source of variation, and the algorithm could be unrobust against different grouping. In our study, however, different grouping resulted only in slight difference in estimates.

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3. Conditional Maximum Likelihood Estimates

For a given gene size δ_j , the likelihood function (3.4) can be written differently as

$$L_{j}(\gamma,\lambda \mid N_{j}) = \binom{N_{j}}{n_{j}} q_{j}^{n_{j}} p_{j}^{N_{j}-n_{j}} \prod_{i=1}^{n_{j}} f(x_{j,i}^{*},\delta_{j}\lambda)$$
 (5.1)

Here f(., .) is defined in (3.1), and $x_{j,1}^{*}, x_{j,2}^{*}, \dots, x_{j,n_j}^{*}$ are the n_j nonzero [0170] observations from N_j genes of size δ_j . Assume there are g different gene sizes, the likelihood function can be written as

$$L = \left(\prod_{j=1}^{g} {N_j \choose n_j} q_j^{n_j} p_j^{N_j - n_j} \right) \left(\prod_{j=1}^{g} \prod_{i=1}^{n_j} f(x_{j,i}^*, \delta_j \lambda) \right) = L_1 \cdot L_2 \quad (5.2)$$

with

$$\sum_{j=1}^8 n_j = n .$$

Assuming the number of observations \boldsymbol{n}_j for each gene size δ_j being fixed, we can obtain the conditional maximum likelihood estimate of λ by maximize L_2 as

$$\hat{\lambda} = \|S\| / \sum_{j=1}^{g} n_j \frac{\delta_j}{1 - e^{-\hat{\lambda}\delta_j}}, \qquad (5.3)$$

where
$$||S|| = \sum_{j=1}^{g} \sum_{i=1}^{n_j} x_{j,i}^* = \sum_{i=1}^{n} x_i^*$$
.

Equation (5.3) reduces to equation (4.2) if we estimate
$$N_j$$
 by $N_j = \frac{n_j}{1 - e^{-\lambda \delta_j}}$.

The proportion of truncated nonessential genes can be calculated as

$$\hat{p} = P(x = 0 \mid non \, essential) = \int_{\Omega} e^{-\lambda \delta} dF(\delta). \tag{5.4}$$

[0172] Here Ω is the set of nonessential genes, which can be approximated by the set of all untruncated genes.

Therefore,

$$\hat{\gamma} = \frac{n}{M} + \hat{p} \tag{5.5}$$

Estimations from the three approaches are very similar as shown in Table 8. If the primary interest is to estimate λ and γ , the conditional MLE approach has the advantage of simplicity. However, in estimating λ , this approach omitted information of \vec{M} , and γ is estimated separately after λ is estimated. Another obvious limitation of this approach is that it can only estimate $\|\vec{N}\|$, the total number of nonessential genes by $\|\vec{n}\|/\hat{r}$. The estimation of \vec{N} by \vec{n}/\hat{r} is not reasonable because even though γ is independent of gene

size, we can not assume the proportion of non-essential genes in different sizes being the same as shown in Figure 17.

Tabl 8. Estimates of γ and λ with the Three Approaches

		Estimates	Bias	SE	95% BCa Confidence intervals
Multivariate Model with					
Exact Gene Sizes	γ	0.843	3.942x10 ⁻³	9.893x10 ⁻³	(0.818, 0.859)
	λ	2.547x10 ⁻³	-1.024x10 ⁻⁵	4.320x10 ⁻⁵	$(2.473, 2.642) \times 10^{-3}$
Multivariate Model with					
Grouped Gene Sizes	γ	0.853	7.221x10 ⁻⁴	8.051x10 ⁻³	(0.835, 0.867)
	λ	2.524x10 ⁻³	2.803x10 ⁻⁶	4.063x10 ⁻⁵	$(2.451, 2.610) \times 10^{-3}$
Conditional Maximum					
Likelihood Estimates	γ	0.828	-7.621x10 ⁻⁵	7.273x10 ⁻³	(0.815, 0.843)
	λ	2.539x10 ⁻³	9.713x10 ⁻⁷	4.058x10 ⁻⁵	$(2.455, 2.618) \times 10^{-3}$

E. DISCUSSION OF ONE DIMENTSIONAL CASE

When the model does not depend on gene size, which can happen for [0173]example, when we study a subset of genes with a fixed size, or in other settings where the distribution is identical, model (2.6) reduces to (2.5). Blumenthal, Dayhiya, and Gross (1978) studies estimations of complete sample size from an incomplete Poisson sample using conditional, unconditional, and modified maximum likelihood functions. The modified likelihood estimation weights the likelihood function and maximizes it.

This approach is similar to providing priors to λ and N. Table 9 presents four types of estimations of N using data randomly selected from the 143 grouped genes. Here M and n are number of genes and number of genes with at least one observed transposon insertions. N_{m-b} is a subset of N_1 in Table 7, which is estimated using model (2.6) with grouped data; N_b is estimated with model (2.5); N_c and N_u are conditional and unconditional estimates of N as described in Blumenthal., Dayhiya, and Gross (1978).

Table 9: Comparison of Estimations with Different Methods

Gene size	М	n	N _{m-b}	N _b	N_u	N _c
[72, 120]	7	2	6	2	3	2
(400 – 410]	44	31	40	37	36	36
(430 – 440]	46	22	38	25	25	26
(470 – 480]	80	42	66	57	56	57
(500 – 510]	54	30	45	39	39	39
(610 – 620]	47	29	39	33	33	34
(640 – 650]	54	35	45	44	43	43
(710 – 720]	50	35	42	41	41	41
(750 – 760]	56	37	46	39	46	40
(770 – 780]	61	43	51	53	52	52
(910 – 920]	60	47	52	53	53	52
(980 – 990]	57	45	49	52	51	51

(1050 – 1100]	137	107	115	117	115	117
(1200 – 1250]	129	100	106	106	106	106
(1400 – 1450]	121	110	111	112	112	112
(2100 – 2150]	23	20	20	20	20	20

[0174] We see that the estimations from the three univariate models are very similar. For fairly large genes, estimations from the multivariate model are similar to those of the univariate models. However, for small genes with high truncation rate, estimations from the multivariate model are larger than estimations from the univariate models. In the univariate models, only the information related to a particular gene size is used and the estimations are obtained separately for each gene size. This approach tends to underestimate N for small genes with sparse observations. The multivariate model uses a prior to enforce the fact that the essentialness of a gene is independent of its size and maximizes the likelihood jointly for all genes. Therefore, it alleviates the underestimation of N for small genes with high truncation rate.

Example 2: lpxC

[0175] Lipid A constitutes the outer layer of the outer membranes of gram-negative bacteria and is essential for bacterial growth. This makes all the enzymes involved in the biosynthesis of this molecule essential for bacterial growth, and therefore ideal targets for drug design. A series of synthetic molecules was previously identified that inhibited the first committed step in lipid A biosynthesis. Onishi H. R., B. A. Pelak, L. S. Gerckens, L. L. Silver, F. M Kahan, M-H Chen, A. A. Patchett, S. M. Galloway, S. A. Hyland, M. S. Anderson, and C. R. H. Raetz. 1996. Science. 274: 980-982. This step is catalyzed by a unique deacetylase (UDP-3-O-[R-3-hydroxymyristoyl]-GlcNAc deacetylase), LpxC.

[0176] UDP-3-O-[R-3-hydroxymyristoyl]-GlcNAc deacetylase (LpxC) is a deacetylase that catalyzes the first committed step of lipopolysaccharide (LPS) biosynthesis in gram negative bacteria. This is the second step following the first

acylation of N-Acetylglucosamine (GlcNAc). This enzyme functions to deacetylate the UDP-3-O-[R-3-hydroxymyristoyl]-GlcNAc. This step was shown to be essential for growth in E. coli wherein a point mutant (EnvA1) expresses an LpxC protein that has reduced activity. Beall B. and J. Lutkenhaus, 1987. Sequence analysis, transcriptional organization, and insertional mutagenesis of the envA gene of Escherichia coli. J. Bacteriol. 169: 5408-5415. A 30% reduction in the amount of LPS on the cell wall of such mutants results in hypersensitivity to antibiotics. Attempts to create null mutants in lpxC were unsuccessful in a number of pathogenic bacteria, indicating that inhibitors of LpxC would be effective antibiotics for a number of gram negative organisms.

[0177] Previously identified inhibitors are chiral hydroxamic acids that had unique hydrophobic aromatic moieties, and were suspected to bind a metal in the active site of the deacetylase. The most potent inhibitor, L-161,240, displayed a minimal inhibitory concentration of about 1 microgram per milliliter against *E. coli*, caused three logs of bacterial killing in 4 hours, and cured mice infected with a lethal intraperitoneal dose of *E. coli*. Considering the very high degree of homology between the *E. coli* and *P. aeruginosa* enzymes, it was initially presumed that an inhibitor of the *E. coli* enzyme might also inhibit the *P. aeruginosa* enzyme. However, this molecule inhibited LpxC from *P. aeruginosa* only at very high concentrations, and even then it did so poorly. It had no effect on bacterial growth in this organism. Thus, there was some question as to whether the *lpxC* homologue had the same function in *P. aeruginosa*, and whether it was essential to *P. aeruginosa* given its decreased sensitivity to the L,161,240 inhibitor.

[0178] Nevertheless, P. aeruginosa lpxC was one nucleic acid identified as being unable to accommodate a transposon insertion in the library depicted in Table 1 (PA4406). To test the essentiality of P. aeruginosa lpxC, we first tested the sensitivity of P. aeruginosa transformants expressing E. coli LpxC following a "promoter swap" integration. Using this technique, we completely shut off expression of the native P. aeruginosa lpxC, while expressing only the E. coli enzyme encoded on a plasmid. This strategy resulted in a P. aeruginosa mutant that was more sensitive to L-161,240. This suggested that the E coli lpxC gene was substituting for the function of the P. aeruginosa gene, and moreover, that there were no duplicate functional homologues in P. aeruginosa that were active in the absence of lpxC.

[0179] Materials. Pseudomonas aeruginosa PAO1 was grown at 37°C in Luria-Bertani (LB) broth (Difco) or plated on sheep blood agar (Remel). Tetracycline at 100 µg/ml in LB media was used to maintain the selection of the integrated plasmid pBEM10 in PAO1. LB broth or agar with 10 µg/ml of tetracycline was used for growing E. coli DH5a (Gibco BRL) and E. coli S-17 transformants. Plasmids pPS72 and pBADHisB were from Promega and Invitrogen, respectively. EDTA, bis-tri buffer, sucrose, arabinose, and DMSO were purchased from Sigma as Ultrapure agents. Yeast extract and Tryptone were obtained from Difco. Restriction enzymes, and T4 DNA Ligase, and their reaction buffers were from New England Biolabs. Polymixin B nonapeptide was from Sigma. The antibiotics, tetracycline, ampicillin, carbenicillin, gentamicin, and kanamycin were all purchased from Sigma. DNA and deduced amino acid information were analyzed using a family of programs included in the Dnastar package. BLASTP was used to search for amino acid similarities among a host of protein databases available on-line through the National Library of Medicine (USA). Altschul, T. F., W. Gish, W. Miller, E. W. Myers, and D. J. Lipman. 1990. Basic local alignment tool, J. Mol. Biol. 215: 403-410.

[0180] DNA manipulations. Standard recombinant DNA procedures were used. Sambrook, J., E. F. Fritsch, and T. Maniatis. 1989. *Molecular cloning: a Laboratory Manual*, 2nd Edition. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory. Primers were designed to the N- and C-terminal regions of the *E. coli* or *P. aeruginosa lpxC* gene that encompassed only the coding region and included *NdeI* and *EcoRI* restriction sites for subsequent cloning. For the *E. coli* gene the primers were (5'-GGGAATTCCATATGATCAAACAAAGGACACTTAAACGT-3' and 5'-CCGGAATTCTTATGCCAGTACAGCTGAAGGCGCT-3') and for *P. aeruginosa* gene they were (5'-

GGGAATTCCATATGATGATCAAACAACGCACCTTGAAGAACAT-3' and 5'-CCGGAATTCCTACACTGCCGCCGCCGGGCGCATATAG-3'). These primers were used in a polymerase chain reaction (PCR) containing either *P. aeruginosa* genomic DNA (10-50 µg) or plasmid pKD6 containing the *E. coli lpxC* gene (1.0 µg) as template (Sorensen, P. G., J. Lutkenhaus, K. Young, S. S. Eveland, M. S. Anderson,

and C. R. H. Raetz. 1996. Regulation of UDP-3-O-[R-hydroxymyristoyl]-Nacetylglucosamine deacetylase in Escherichia coli. The second enzymatic step of lipid A biosynthesis. J. Biol. Chem. 271 (42): 25898-25905). The lpxC genes were amplified using Pwo DNA polymerase (Roche) in a 100 µl reaction mixture containing 200 µM concentration of each dNTP and 0.5 µM concentration of each primer for 30 cycles (94°C denaturation, 55°C annealing, and 72°C polymerization (according to the manufacturer's instructions). The PCR products were purified with the Qiaquick PCR Purification Kit from Qiagen (according to the manufacturer's instructions) and digested with NdeI and EcoRI restriction enzymes at sites introduced by the primer sequences. Bands of the correct sizes predicted for the lpxC genes were separated by gel electrophoresis, and the excised DNA purified using the Qiaquick Gel Extraction Kit from Qiagen (according to the manufacturer's instructions). The purified DNA was ligated into the T7 expression vector (Studier, F. W., A. H. Rosenberg, J.J. Dunn, and J. W. Dubendorff. 1990. Use of T7 RNA polymerase to direct expression of cloned genes. Methods Enzymol. 185: 60-89) pET21b (Novagen), that had been cut in the multiple cloning site with the same enzymes, transformed into DH5\alpha and plated on LB agar containing ampicillin (250 µg/ml). The resulting clones had their DNA sequenced to confirm the fidelity of the PCR reactions before it could be transferred into the expression strain. Subcloning of these fragments into other vectors was carried out as needed for expression in various backgrounds. These included pEX18T (cbR) for allelic exchange mutagenesis in P. aeruginosa (Schweizer, H. P and T. T. Hoang. 1995. An improved system for gene replacement and xylE fusion analysis in Pseudomonas aeruginosa. Gene 158 (1): 15-22), pDN19 (tetR) for low copy number complementation of E. coli JBK-1 (Nunn, D., S. Bergman, and S. Lory. 1990. Products of three accessory genes, pilB, pilC, and pilD, are required for biogenesis of Pseudomonas aeruginosa pili. J. Bacteriol. 172 (6): 2911-2919), and pUCP30T (gmR) for P. aeruginosa 'promoter swap' mutant complementation (Schweizer, H. P., T. R. Classen, and T. Hoang. 1996. Improved methods for gene analysis and expression in Pseudomonas. In: Nakazawa, T., K Furukawa, D. Haas, S. Silver. (Eds.) Molecular Biology of Pseudomonas. American Society for Microbiology, Washington, DC. pp. 229-237).

[0181] Construction of pBEM10 and 'promoter swap' mutagenesis. Plasmid pPW101 was made by ligating oriT, the region that encodes conjugative plasmid transfer, into pSP72 (Promega). oriT had been amplified from plasmid pEX100T (Schweizer and Hoang, 1995, supra) with an introduction of an NdeI and an AatII restriction sites. To create the lpxC 'promoter swap' vector, pBEM10, the following different DNA pieces were amplified and sequentially ligated into pPW101. These included the tetracycline resistance marker (tetR) from plasmid pUCP26 (Olsen, R. H., G. DeBusscher and R. R. McCombie. 1982. Development of broad-host-range vectors and gene banks: self-cloning of the Pseudomonas aeruginosa PAO chromosome. J. Bacteriol. 150: 60-69), the araBAD promoter from the plasmid pBAD HisB (Invitrogen) with an altered ribosome binding site (rbs) (Guzman, L.M., D. Belin, M. J. Carson, and J. Beckwith. 1995. Tight regulation, modulation, and high-level expression by vectors containing the arabinose pBAD promoter. J Bacteriol. 177 (14):4121-4130), the araC gene, also from pBAD HisB (Lee, N. 1980. Molecular aspects of ara regulation. In The Operon. J. H. Miller and W. S. Reznikoff, eds. Cold Spring Harbor, NY. Cold Spring Harbor Laboratory, pp. 389-410; and Schleif, R. S. 1992. DNA looping. Ann. Rev. Biochem. 61: 199-223), and the first 340 base pairs of the P. aeruginosa lpxC gene. The tetR marker was amplified using a forward primer that introduced a BgIII site (5'- AGATCTCAAGGGTTGGTTTGCGCA-3') and a reverse primer that introduced an EcoRI site (5'-

GAATTCTCATGTTTGACA-3'). The *ara*BAD promoter and *ara*C gene were amplified as one piece from the pBAD HisB vector. The forward primer introduced an *Xho*I site (5'-CTCGAGGCATGCATAATGTGCCTGTC-3') and the reverse primer introduced a *Hind*III site (5'-

AAGCTTCTCCTGTTAGCCCAAAAAAACG-3'). The rbs was altered from its original AGGAG to CTTCT. The following primer set was used to make these changes and introduced an upstream *Bss*HII site (5'-

GCGCGCGACGAAAGTAAACCCAC

TGG-3') and a downstream HindIII site (5'-

AAGCTTATTCAGAAGGTTAGCCCAAAA AAACGGG-3'). The first 340 bases of

PAO1 *lpxC* were amplified from PAO1 genomic DNA. The forward primer introduced a *Hind*III site (5'-AAGCTTATGATCAAACAACGCACCTT-3') and the reverse primer introduced an *Xba*I site (5'-TCTAGAAGCGCTGCCATCCATGATCGG-3'). These pieces were then ligated into pPW101 to form the final product, pBEM10, which was used for the 'promoter swap' mutagenesis of *lpx*C. The 'promoter swap' scheme is a homologous recombination strategy, whereby transformation of pBEM10 into *P. aeruginosa* removed the native *lpxC* promoter and placed the tightly regulated *ara*BAD promoter upstream of the chromosomal copy of *lpxC*, allowing modulation of its expression by the use of a simple sugar, arabinose (Figure 3). In the absence of arabinose the *lpxC* was effectively shut off, and expression was inducible by addition of arabinose. Such mutants were selected in the presence of arabinose, and if *lpxC* is essential, these mutants would not be viable in media that is not supplemented with arabinose, but fully capable of growth in the presence of arabinose.

[0182] Growth curves. Bacterial cultures were prepared by diluting stationary phase overnight cultures to an OD₆₀₀ of 0.1 in 5 ml of LB. The inhibitor, L-161,240, was resuspended in DMSO to a final concentration of 10mg/ml and added to the bacterial cultures to a final concentration of 50 μg/ml or 10 μg/ml. In the samples without inhibitor, DMSO was added to keep the final concentration of DMSO equivalent between samples. The cultures were incubated with shaking and 0.8 ml was taken for OD₆₀₀ readings over the course of the experiment. DH5α, PA01, and PA0200 (Schweizer, H. P. 1998. Intrinsic resistance to inhibitors of fatty acid biosynthesis in *Pseudomonas aeruginosa* is due to efflux: application of a novel technique for generation of unmarked chromosomal mutations for the study of efflux systems. Antimicrob. Agents Chemother. 42: 394-398) were all grown at 37°C. In the cases where temperature sensitive JBK strains were being assayed, the cultures were grown at 42°C for both the overnight and the time course cultures.

[0183] Outer membrane permeabilization. Polymixin B nonapeptide (Sigma) was prepared as a suspension in DMSO at 3 mg/ml final concentration. Erythromycin and Tetracycline were resuspended in DMSO to a final concentration of 250 mg/ml and 125 mg/ml, respectively. L-161,240 was prepared as above in DMSO to a final

concentration of 10mg/ml. These DMSO antibiotic solutions were individually added to LB to the appropriate final concentration and mixed. Polymixin B nonapeptide was then added to the appropriate samples and mixed. DMSO was added to each sample to keep the final concentration of DMSO equivalent between samples. A stationary phase overnight culture of PA01 was added to each sample to bring the final concentration to 0.1 OD_{600} . Samples were removed for OD_{600} determinations every 1-2 hours for 6.5 hours and the data from these time points were plotted.

[0184] MIC determinations for 'promoter swapped' mutants. Single colonies of DH5 α , PA01 and each promoter swap strain were picked and grown in LB at 37°C with shaking for approximately 4 hours. Assuming that an OD₆₀₀ reading of 1.0 is equivalent to 10^9 cells/ml, dilutions were made of all cultures to 5×10^5 cells/ml. 200 μ l of each diluted culture was added to each well where a two-fold serial dilution of inhibitor had been placed. The 96-well plates were incubated at 37°C overnight and their OD₆₀₀ determined using the Spectramax Plus (Molecular Devices) plate reader.

[0185] To confirm the effect of the arabinose-sensitive promoter in regulating the lpxC expression in the swapped mutants, MIC determinations were performed as above, except that arabinose was added to induce expression of the chromosomal locus and override the effects of the plasmid borne lpxC. In this case the stationary-phase overnight bacterial culture was diluted to $5x10^5$ cells/ml in LB containing Arabinose to a final concentration of 0.2% (a 20% stock made up in water).

RESULTS AND DISCUSSION:

[0186] Homology between the *E. coli* and the *P. aeruginosa* LpxC enzymes. Using protein analysis software, this study and others have compared the deduced amino acid sequence of LpxC from both *E. coli* and *P. aeruginosa* (Hyland, S.A., S. S. Eveland, and M. S. Anderson. 1997. Cloning, expression, and Purification of UDP-3-O-Acyl-GlcNAc Deacetylase from *Pseudomonas aeruginosa*: a metalloamidase of the lipid A biosynthesis pathway. J. Bacteriol. 179 (6): 2029-2037). This comparison revealed

82% similarity and 57% identity shared between the two sequences. This homology was found over the entire length of the protein sequence (data not shown). Significant homology with other known acetyl- or acyltransferases was not found, suggesting that LpxC is unique among acetyltransferases. The two proteins also share a total of five fully conserved Histidine residues that are presumed to be responsible for the zinc metal cofactor coordination. It was therefore expected that an inhibitor that functions by chelating the metal cofactor away would affect both enzymes similarly.

[0187] LpxC is essential for growth in P. aeruginosa. Since the hydroxamate inhibitor was effective in preventing growth of E. coli, but completely ineffective against P. aeruginosa, there was a possibility that LpxC was not essential in P. aeruginosa. This could be as a result of the presence of another enzyme that catalyzed a similar function. If that were the case, elimination of the LpxC function should be possible without inhibiting bacterial growth. A thorough analysis of the P. aeruginosa genome sequence revealed only one LpxC homologue. An attempt to disrupt the function of this LpxC homologue was made by conjugating wild type PAO1 with a suicide vector (pEX18T) carrying lpxC whose BamHI - SalI fragment had been replaced with a gentamicin cassette. However, P. aeruginosa null mutants could not be established by this method. In several attempts a few gentamicin resistant transconjugants were obtained, but in all these cases allelic replacement of the chromosomal lpxC by the defective copy had not occurred. Instead, a gene duplication had occurred, placing the suicide vector and the disrupted copy next to the wild type allele (data not shown). This could be demonstrated by the carbenicillin resistance and sucrose sensitivity acquired by these trans-conjugants, both of which are encoded on the suicide vector. These data indicated a strong negative selection for the sought after disruption of lpxC suggesting that lpxC is essential for growth. To confirm this, an experiment was carried out whereby the trans-conjugants were transformed with either lpxC on a low copy, replicating vector, or vector alone. In 100% of lpxC transformants, resolution of the gene duplication as demonstrated by the loss of carbenicillin resistance and sucrose sensitivity was observed, as opposed to no such resolution among those

transformed with vector alone. These results suggested that the wild type genomic allele could be disrupted if a functional copy was present on the transforming plasmid.

[0187] In another attempt at demonstrating essentiality of LpxC in *P. aeruginosa*, the 'promoter swap' strategy as described in materials and methods was carried out. 'Promoter swapped' pseudomonas mutants were fully capable of growth in the presence of arabinose when the arabinose sensitive *lpxC* promoter was turned on, but completely incapable of growth in the absence of this inducer. This further confirmed that in *P. aeruginosa*, just as in *E. coli*, LpxC is essential for growth.

[0188] E. coli expressing LpxC from P. aeruginosa is more resistant to L-161, 240. The E. coli strain JBK-1/pKD6 contains the chromosomal lpxC gene disrupted with a kan element and a wild type copy of E. coli lpxC on the temperature-sensitive replicon pKD6. The strain was constructed as described by Sorensen et al., 1996. Since lpxC is essential for growth, this strain is not viable at 42°C because the functional copy is on the temperature sensitive replicon. Transforming JBK-1/pKD6 with lpxC from either E. coli or P. aeruginosa on a non-temperature-sensitive replicon (pKD19, TetR) and selecting at 42°C, produced transformants that were viable at 42°C, tetracycline resistant, and kanamycin sensitive. This result indicated that lpxC from P. aeruginosa could be expressed in the E. coli background, and was capable of substituting for the missing chromosomal copy. An unexpected result was that whereas the JBK-1 carrying the lpxC copy from E. coli was still sensitive to killing by a slightly higher concentration of L-161,240, the JBK-1 carrying the lpxC copy from P. aeruginosa was resistant to up to 50 µg/ml, about 50 times above the MIC of the wild type organisms (data not shown). This suggested that the P. aeruginosa enzyme was uniquely resistant to this inhibitor. It also meant that this resistance was the reason for the failure to inhibit growth of P. aeruginosa, and not reduced permeability, or efflux or modification of drug by the pseudomonal enzymes. This, in turn, suggests that a program designed to search for inhibitors for the pseudomonal enzyme should be based on screening directly on that enzyme, and not the surrogate enzyme from E. coli.

[0189] L-161, 240 is a substrate for the major drug efflux pump of P. aeruginosa. The completed P. aeruginosa genome reveals genes for at least nine homologous, multicomponent, multidrug efflux systems (Stover et al., 2000, Complete genome sequence of Pseudomonas aeruginosa PA01, an opportunistic pathogen, Nature 406: 959-64). However the only one that is constitutively expressed to a high degree in the wild type strains is MexAB-OprM (Kohler, T., M. Michea-Hamzehpour, and U. Henze. 1997. Characterization of MexE-MexF-OprN, a positively regulated multidrug efflux system of Pseudomonas aeruginosa. Mol. Microbiol. 23: 345-354). Therefore, mutants of this efflux system can be used to evaluate the consequences of diminished efflux pump activity. These mutants would be expected to be highly sensitive to a number of antibiotics. Such a mutant, PAO 200, has been isolated (Schweizer, 1998, supra), and whereas it shows a higher level of sensitivity to a number of antibiotics (Westbrock-Wadman, S. D. R. Sherman, M. J. Hickey, S. N. Coulter, Y. Q. Zhu, P. Warrener, L. Y. Nguyen, R. M. Shawar, K. R. Folger, and C. K. Stover . 1999. Characterization of a Pseudomonas aeruginosa Efflux Pump Contributing to Aminoglycoside Impermeability. Antimicrobial Agents and Chemotherapy. 43 (12): 2975-2983), it was not more sensitive to L-161,240 (Figure 4). This suggests that this drug compound is not a substrate for this efflux system in P. aeruginosa.

[0190] P. aeruginosa is not less permeable to L-161,240. Low permeability of the outer membrane is a major contributing factor to the observed high levels of intrinsic drug resistance in P. aeruginosa (Nikaido, H. 1998. The role of outer membrane and efflux pumps in the resistance of gram-negative bacteria. Can we improve access? Drug Resistance Updates. 1: 93-98). This low permeability is due to the fact that P. aeruginosa lacks the homolog of the relatively efficient, trimeric porins like OmpF. P. aeruginosa has, instead, OprF, the OmpA homolog, which produces channels only when it is folded into a rare conformation, and only a small fraction of these channels occurs in the open conformation. As is usually the case with P. aeruginosa it was assumed that the reason L-161,240 was ineffective against P. aeruginosa was the lack of permeability of the outer membrane to this inhibitor. Polymixin B nonapeptide (PMBN), a derivative of Polymixin B that lacks the fatty acid tail, is capable of binding

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to the polyanionic LPS molecules and disrupting the bilayer structure, thus increasing the permeability of the outer membrane. PMBN has been used this way to permeabilize the outer membrane of many gram-negative bacteria (Vaara, M. and T. Vaara. 1983. Sensitization of gram-negative bacteria to antibiotics and complement by a nontoxic oligopeptide. Nature 303: 526-528), including *P. aeruginosa* (Vilianen, P. and M. Vaara, 1984. Susceptibility of gram-negative bacteria to polymixin B nonapeptide. Antimicro Agents Chemother. 25: 701-705) and effectively sensitize them to lipophilic antibiotics. Unlike the acylated polymixin B, PMBN is not cidal. In order to determine the effect of outer membrane exclusion of L-161,240, we exposed *P. aeruginosa* to PMBN in combination with L-161,240, and with other lipophilic antibiotics as positive controls. Whereas PMBN lowered the MIC of tetracycline for *P. aeruginosa* more than 16 fold, the sensitivity towards L-161,240 remained unchanged (Figure 5). This, together with the *E. coli* expression data indicated that permeability was not a major factor causing the inability of L-161,240 to inhibit pseudomonal growth.

[0191] P. aeruginosa expressing only E. coli LpxC is more sensitive to L161-240 than wild type. Using the 'promoter swap' technique as described in the methods, it was possible to replace expression from the wild type chromosomal copy of P. aeruginosa lpxC, with expression solely from a plasmid borne copy. For this experiment, 'promoter swapped' P. aeruginosa was transformed with either vector containing P. aeruginosa lpxC ("PA Swap #1"), or vector containing E. coli lpxC ("PA Swap #2'). The transformants were then exposed to various concentrations of L-161,240 for MIC determination. Transformants expressing the E. coli enzyme only were much more sensitive to the inhibitor compared to organisms expressing the P. aeruginosa enzyme (Figure 6). These transformants were sensitive enough to be comparable with the sensitivity seen in E. coli. Since the validity of this observation relied on the un-induced arabinose-sensitive promoter to shut down expression from the chromosomal copy of lpxC, it was necessary to demonstrate how effectively this happens. To do that, MIC determinations were performed as above, except that arabinose was added to induce expression of the chromosomal locus. For this experiment stationary-phase overnight bacterial cultures were diluted to 5x10⁵ cells/ml in LB containing 0.2% arabinose. In this case all the transformants, regardless of what gene the vector contained, were resistant to killing due to the expression of the

chromosomal copy of *P. aeruginosa lpxC*. This confirmed that certain intrinsic properties of the *P. aeruginosa* enzyme are resistant to inhibition by this hydroxamate inhibitor. It also confirmed that neither reduced uptake, efflux, nor modification of the inhibitor play a significant role in this observed resistance. Considering the very high similarity between the two enzymes, this finding was not expected.

[0192] But on further examination and analysis of existing data, it was possible to recognize some inherent differences that might explain this finding. Whereas both these enzymes share five conserved Histidine residues, the E. coli enzyme has two more Histidines that have no counterparts in the P. aeruginosa enzyme. This is an important difference because these residues are probably involved in the metal cofactor coordination. It was also observed earlier that whereas the E. coli enzyme is not sensitive to EDTA, the P. aeruginosa enzyme was significantly inhibited by as little as $2 \mu M$ EDTA. Evidence that the *E. coli* enzyme is also a metalloenzyme is that the envA1 mutation, which has one of the conserved Histidines (His 19) replaced by a Serine, is sensitive to EDTA. It was because of these observations that these investigators suggested that the E. coli enzyme has a more stably bound metal than that of the EnvA1 mutant protein, and thus it is less accessible to EDTA than the wild type P. aeruginosa enzyme. These observations suggest that the Histidine 'patch' that is involved in the metal coordination is not similar between the two enzymes. It is conceivable therefore that since the inhibitor works by chelating the metal cofactor away from the enzyme, each 'patch' has unique features that result in disparate reactivities towards the inhibitor. It is also important to consider the findings of Wyckoff et al., 1998. Hydrocarbon rulers in UDP-N-acetylglucosamine acyltransferases. J. Biol. Chem. 273 (49): 32369-32372. These investigators found that LpxA, the first enzyme of lipid A biosynthesis, is very selective for the length of its acyl donor substrates. Whereas E. coli LpxA prefers R-3-hydroxymyristoyl-ACP to R-3-hydroxydecanoyl-ACP, P. aeruginosa LpxA prefers the opposite. The products of the LpxA reaction therefore differ in the carbon chain length of their lipid moieties between the two bacteria. Since the product of the LpxA reaction is the substrate of the LpxC reaction, this observation suggests that the two LpxCs would have substrate binding pockets of different sizes to accommodate the different size substrate. That

would, in turn, suggest that inhibitors that have to occupy that active site would be unique for each enzyme.

Examples 3-7: ispA, ispB, uppS, aroC, aroK, and metK

[0193] Several more candidate genes from the HTTIM gene database were tested for essentiality using a single crossover knock-out strategy. The *Pseudomonas* genes targeted for knocking out were *ispA*, *ispB*, *uppS*, *metK*, *aroC*, and *aroK*. To attempt knock-outs, regions of about 300 bp were cloned into the vector pPW120. These regions were selected so that known active site residues (or highly conserved residues likely to be essential for enzyme function) would be separated after generation of a single-crossover knock-out. The regions were (numbering from the start codon): *ispA*, 283-594; *ispB*, 319-610; *uppS*, 103-402; *metK*, 415-732; *aroC*, 385-684; *aroK*, 175-375.

[0194] The pPW120 vector carries an E. coli origin of replication, but not a Pseudomonas origin of replication, making it a suicide vector. It also carries an origin of conjugal transfer and antibiotic resistance genes for tetracycline and ampicillin. An E. coli donor strain (SM10) carrying the pPW120 knockout constructs was incubated with Pseudomonas strain PAO1 to allow conjugal transfer, and recombinants were selected by plating onto media containing tetracycline at $100 \,\mu g/mL$ and chloramphenicol at $10 \,\mu g/mL$. Pseudomonas recombinants will be resistant to this antibiotic mixture while wild-type PAO1 and the E. coli donor strain will be sensitive. Aromatic amino acid recombinants (aroC and aroK) were then tested for auxotrophy by plating onto minimal media with and without phenylalanine, tryptophan, tyrosine, and folic acid at $100 \,\mu g/mL$ while maintaining tetracycline selection. The genes ispB, uppS and metK did not yield recombinants, demonstrating that they are essential genes in all media conditions, while ispA yielded slow-growing recombinants (suggesting that this gene may nevertheless be an "important" gene according to the invention).

[0195] For ispA, ispB, uppS, and metK, the conjugation procedure was also done in the presence of the complementing plasmid pBAD/HisP. This plasmid has both E. coli and Pseudomonas origins of replication, an antibiotic resistance gene for carbenicillin, and an arabinose-inducible copy of the full-length wild-type gene. In this way,

recombinants with the chromosomal copies of *ispA*, *ispB*, *uppS*, and *metK* knocked out could be isolated since the vector copy would provide complementation.

[0196] The genes *ispB*, *uppS*, and *metK* are novel with regard to *P. aeruginosa*. The gene *ispB* (PA4569, ranging from 5116864 to 5117832 in the genome), has 67% similarity/52% identity to IspB in *E. coli*, and was assigned to the function class concerned with biosynthesis of cofactors, protein groups and carriers, and energy metabolism, with a confidence level of 2. It is thought to be involved in the pathway of ubiquinone biosynthesis.

[0197] The gene uppS (PA3652, ranging from 4091654 to 4090899), coding for undecaprenyl pyrophosphate synthetase, has 69% similarity/57% identity to the uppS gene in E. coli, and was assigned to the function class involved in biosynthesis of cofactors, protein groups and carriers, cell wall and capsule, with a confidence level of 2. It is separated by one gene (cdsA) from dxr, which is involved in the synthesis of isopentenyl diphosphate, a precursor of undecaprenol phosphate.

[0198] The gene metK (PA0546, ranging from 604896 to 603706) had never been characterized in P. aeruginosa, although it is 82% similar/72% identical to MetK in E. coli. The gene encodes methionine adenosyltransferase (adomet synthetase) which is involved specifically in methionine metabolism, and was originally assigned to a function class of amino acid biosynthesis and metabolism and central intermediate metabolism with a confidence level of 2.

Example 8: rrF

[0199] The essentiality of the *P. aeruginosa rrF* (PA3653, ranging from 4092227 to 4091670) gene was tested using the promoter swap methodology disclosed herein. The N-terminus region (position 1-327) of the gene encoding the ribosome recycling factor (frr) was cloned into the plasmid vector pBEM10. A single crossover was constructed as described above for lpxC. Recombinants were unable to grow in the absence of arabinose, confirming the essentiality of this gene. The *rrf* gene encodes ribosome recycling factor, alternatively known as ribosome releasing factor, assigned to the functional class pertaining to translation, post-translational modification and

degradation with a confidence level of 1. Although this gene was previously known in *Pseudomonas aeruginosa*, confirming the essentiality of known genes using the methods disclosed herein will reveal new utilities for such genes as targets for the identification and design of new antibacterial drugs.

PCT/US02/35518 WO 03/089572

RANUMBEN	GenBankilD		GenevName	AND Geneal Name & State of the
PA0001	9945819	chromosomal replication initiator protein DnaA	dnaA	:
PA0004		DNA gyrase subunit B	gyrB	
PA0006	9945824	conserved hypothetical protein		iyaeD
PA0008	9945826	glycyl-tRNA synthetase beta chain	glyS	:
PA0009	9945827	glycyl-tRNA synthetase alpha chain	glyQ	
PA0011		probable 2-OH-lauroyltransferase	}	
PA0015		hypothetical protein	:	
PA0022	9945841	conserved hypothetical protein	1	yrdC
PA0026		hypothetical protein	1	
PA0033		hypothetical protein		
PA0035		tryptophan synthase alpha chain	trpA	
PA0038	9945859	hypothetical protein	1	
PA0036	9945860	hypothetical protein	<u> </u>	
PA0039		hypothetical protein		
PA0042		hypothetical protein		
PA0047		hypothetical protein	1	
PA0052	9945076	hypothetical protein		
	9945070	conserved hypothetical protein	<u> </u>	yjil
PA0054	0045979	hypothetical protein		
PA0055		hypothetical protein		
PA0058	0045992	osmotically inducible protein OsmC	osmC	
PA0059	0045002	conserved hypothetical protein		
PA0060		hypothetical protein	1	1
PA0061		hypothetical protein		
PA0065		hypothetical protein		
PA0068	9943092	conserved hypothetical protein		
PA0069		hypothetical protein	 	
PA0070 PA0080		hypothetical protein	 	
PA0080		hypothetical protein	i	
PA0094		hypothetical protein	1	
PA0094		hypothetical protein	 .	
PA0100		hypothetical protein	1	
PA0105	0045032	cytochrome c oxidase, subunit II	сохВ	icoll
PA0109	9945936	hypothetical protein	<u> </u>	
PA0103		hypothetical protein		
PA0113	9945940	probable cytochrome c oxidase assembly fac	to	
PA0114	9945941	conserved hypothetical protein	·	
PA0115		conserved hypothetical protein	 	elaA
PA0116		hypothetical protein	T	,
PA0119		probable dicarboxylate transporter		
PA0120		probable transcriptional regulator	· [
PA0120	9945952	hypothetical protein		
PA0124		hypothetical protein		
PA0125		conserved hypothetical protein	1	phnA
PA0128		hypothetical protein	 	ľ
	9945960	probable transcriptional regulator		
PA0133		hypothetical protein	<u> </u>	
PA0135	0045060	alkyl hydroperoxide reductase subunit C	ahpC	
PA0139	1 9940908	3 probable nucleoside hydrolase	, , , , , , , , , , , , , , , , , , , ,	<u></u>
PA0143		hypothetical protein		<u> </u>
PA0145	1 994597	probable sigma-70 factor, ECF subfamily	·	1
PA0149	334530	Albiopanie sigilia-10 lactor, Lot subtaining	<u></u>	

PA0154	9945985 protocatechuate 3,4-dioxygenase, alpha sut	ounpcaG	
PA0159	9945991 probable transcriptional regulator		en alle de la company de la co
PA0161	9945993 hypothetical protein		:
PA0167	9945999 probable transcriptional regulator		
PA0170	9946003 hypothetical protein	:	
PA0171	9946004 hypothetical protein		:
PA0182	9946016 probable short-chain dehydrogenase		yjgl
PA0183	9946017 arylsulfatase	atsA	
PA0184	9946018 probable ATP-binding component of ABC tr	ans	atsC
PA0187	9946021 hypothetical protein	;	
PA0188	9946022 hypothetical protein	1	:
PA0200	9946035 hypothetical protein		
	9946037 probable amidase		i
PA0202	9946038 probable binding protein component of ABC	tria	
PA0203	9946039 probable permease of ABC transporter		i
PA0204	9946040 probable permease of ABC transporter	i	
PA0205	9946040 probable permease of ABC transporter		
PA0207	9946042 probable transcriptional regulator 9946045 conserved hypothetical protein		mdcB
PA0209	9946045 conserved hypothetical protein	mdcD	111000
PA0211	9946047 malonate decarboxylase beta subunit	indeb	mdcG
PA0213	9946049 hypothetical protein		madM
PA0216	9946052 probable transporter		imadivi
PA0233	9946071 probable transcriptional regulator		
PA0236	9946074 probable transcriptional regulator		
PA0238	9946076 hypothetical protein		
PA0243	9946082 probable transcriptional regulator		
PA0244	9946083 hypothetical protein		D2
PA0245	9946084 3-dehydroquinate dehydratase	aroQ2	aroD2
PA0250	9946090 conserved hypothetical protein		
PA0251	9946091 hypothetical protein		
PA0258	9946098 hypothetical protein		
PA0260	9946101 hypothetical protein		
PA0261	9946102 hypothetical protein		
PA0264	9946105 hypothetical protein		<u> </u>
PA0273	9946115 probable MFS transporter		
PA0279	9946122 probable transcriptional regulator		ydfF
PA0280	9946123 sulfate transport protein CysA	cysA	
PA0284	9946127 hypothetical protein		
PA0309	9946155 hypothetical protein		
PA0311	9946157 hypothetical protein		
PA0320	9946167 conserved hypothetical protein		
PA0330	9946178 ribose 5-phosphate isomerase	rpiA	
PA0332	9946180 hypothetical protein		
PA0336	9946184 conserved hypothetical protein		ygdP
PA0339	9946187 hypothetical protein		
PA0341	9946190 prolipoprotein diacylglyceryl transferase	lgt	umpA
PA0342	9946191 thymidylate synthase	thyA	
PA0350	9946200 dihydrofolate reductase	folA	tmrA
PA0358	9946208 hypothetical protein		
	9946213 ferredoxin [4Fe-4S]	fdx1	
PA0362	9946214 phosphopantetheine adenylyltransferáse	coaD	kdtB
PA0363		:	
PA0369	9946220 hypothetical protein		yhhF
PA0370	9946222 conserved hypothetical protein	<u> </u>	17

PA0373	9946225 signal recognition particle receptor FtsY	ftsY	
PA0376	9946228 sigma factor RpoH	rpoH	
PA0377	9946229 hypothetical protein		į
PA0380	9946232 conserved hypothetical protein	:	1
PA0384	9946237 hypothetical protein		
PA0398	9946252 hypothetical protein	:	1
PA0402	9946256 aspartate carbamoyltransferase	уругВ	j
PA0403	9946257 transcriptional regulator PyrR	ipyrR	i
PA0404	9946258 conserved hypothetical protein		iyqgF
PA0404	9946259 conserved hypothetical protein	<u> </u>	yqgE
PA0405	9946262 glutathione synthetase	gshB	
PA0407	9946267 methyltransferase PilK	pilK	
	9946271 probable transcriptional regulator		chpD
PA0416	9946278 conserved hypothetical protein		
PA0422	9946283 outer membrane protein OprM precursor	oprM	
PA0427	9946290 hypothetical protein		
PA0433	9946300 hypothetical protein	<u> </u>	
PA0442	9946301 probable transporter		
PA0443	9946304 probable transposase		
PA0445	9946305 conserved hypothetical protein		
PA0446	9946307 probable transcriptional regulator		
PA0448	9946312 hypothetical protein		
PA0453	9946316 probable cold-shock protein		
PA0456	9946327 hypothetical protein		
PA0466	9946336 hypothetical protein	<u> </u>	<u>-</u>
PA0474	9946337 probable transcriptional regulator	<u> </u>	
PA0475	9946339 probable transcriptional regulator		
PA0477	9946341 probable transcriptional regulator		
PA0479	9946351 conserved hypothetical protein		yfiM
PA0488	9946352 probable phosphoribosyl transferase		
PA0489	9946353 hypothetical protein		
PA0490	9946356 probable biotin-requiring enzyme		
PA0493	9946362 hypothetical protein	· - - [
PA0498 PA0501	9946365 8-amino-7-oxononanoate synthase	bioF	
	9946366 probable biotin biosynthesis protein bioH		bioH
PA0502	9946367 probable biotin synthesis protein BioC		bioC
PA0503	9946368 dethiobiotin synthese	bioD	
PA0504	9946369 hypothetical protein	·	
PA0505	9946379 heme d1 biosynthesis protein NirL	nirL	
PA0514	9946393 transcriptional regulator Dnr	dnr	
PA0527	9946397 probable glutamine amidotransferase		
PA0531	9946402 probable transcriptional regulator		
PA0535	9946407 hypothetical protein		
PA0540	9946409 conserved hypothetical protein		yqjC
PA0542	9946410 hypothetical protein		
PA0543	9946411 hypothetical protein		
PA0544	9946414 methionine adenosyltransferase	metK	
PA0546	9946418 conserved hypothetical protein		ygbM
PA0550	9946420 phosphoglycerate kinase	pgk	
PA0552	9946422 hypothetical protein	<u> </u>	
PA0553	9946424 fructose-1,6-bisphosphate aldolase	:fda	fbaA, cbbA, cfxB
PA0555	0046429 conserved by a thorizon protein	i	yhiN
PA0559	9946428 conserved hypothetical protein		

DA0562	0046432 cons	erved hypothetical protein	, , , , , , , , , , , , , , , , , , ,	
PA0563				
PA0565		erved hypothetical protein	} 	jyqaE
PA0567		erved hypothetical protein	! 	iyqaL
PA0570		thetical protein	; :	
PA0571		thetical protein	- 	
PA0574		thetical protein	<u> </u>	
PA0578		erved hypothetical protein	· · · · · · · · · · · · · · · · · · ·	
PA0579			rpsU	
PA0580	9946451 O-sia	aloglycoprotein endopeptidase	gcp	ygjD
PA0582		droneopterin aldolase	folB	
PA0585		thetical protein	<u> </u>	
PA0589		served hypothetical protein		glpE
PA0591	9946463 cons	served hypothetical protein		lapaG
PA0593	9946465 pyrid	doxal phosphate biosynthetic protein PdxA	pdxA	
PA0594	9946466 pept	idyl-prolyl cis-trans isomerase SurA	surA	
PA0595	9946467 orga	nic solvent tolerance protein OstA precurs	ostA	imp
PA0607	9946481 ribul	ose-phosphate 3-epimerase	rpe	dod
PA0610	9946484 trans	scriptional regulator PrtN	prtN	
PA0611	9946485 trans	scriptional regulator PrtR	prtR	
PA0613		othetical protein		
PA0614		othetical protein		
PA0617	9946492 prob	pable bacteriophage protein		•
PA0626		othetical protein		
PA0627	9946502 cons	served hypothetical protein		
PA0630		othetical protein		
PA0632		othetical protein		
PA0635	9946511 hypo	othetical protein		
PA0639	9946515 cons	served hypothetical protein		
PA0642	9946518 hypo	othetical protein	•	
PA0643		othetical protein	-	
PA0644	9946520 hypo	othetical protein	1	
PA0646	9946523 hype	othetical protein	!	
PA0647		othetical protein	1	
PA0648		othetical protein	!	
PA0652	9946529 tran	scriptional regulator Vfr	vfr	
PA0653		served hypothetical protein	<u> </u>	lyhfA
PA0655	9946532 hyp	othetical protein	1	
PA0660	9946538 hyp	othetical protein	<u> </u>	
PA0661	9946539 con	served hypothetical protein	1	
PA0665	9946543 con	served hypothetical protein	1	yadR
PA0678	9946558 prof	bable type II secretion system protein	1	hxcU
PA0679	9946559 hyp	othetical protein	1	hxcP
PA0680	9946560 pro	bable type II secretion system protein		hxcV
PA0684	9946564 pro	bable type II secretion system protein	{	hxcZ
PA0686	9946566 pro	bable type II secretion system protein		hxcR
PA0687	9946567 pro	bable type II secretion system protein		hxcS
PA0689		pothetical protein	i	
PA0697		pothetical protein		
PA0698		pothetical protein	1	
PA0700		pothetical protein		
PA0702		pothetical protein		
11 OU (UC		bable amidase		

DA0705 -:	0046588	probable glycosyl transferase	!	migA
PA0705		probable transcriptional regulator		- 1 1
PA0708				
PA0709		hypothetical protein	gloA2	
PA0710 :		lactoylglutathione lyase	gloAz	
PA0712 :		hypothetical protein	·	
PA0714 :		hypothetical protein		
PA0715		hypothetical protein		
PA0716 i		hypothetical protein		
PA0717	9946601	hypothetical protein of bacteriophage Pf1	<u> </u>	
PA0720		helix destabilizing protein of bacteriophage Pf		
PA0728		probable bacteriophage integrase		
PA0729		hypothetical protein		
PA0730	9946615	probable transferase		
PA0733	9946618	probable pseudouridylate synthase		rsuA
PA0734	9946619	hypothetical protein		
PA0738	9946624	conserved hypothetical protein		:
PA0742	9946628	hypothetical protein		
PA0759	9946647	conserved hypothetical protein		
PA0763		anti-sigma factor MucA	mucA	
PA0767	9946655	GTP-binding protein LepA	lepA	
PA0768		signal peptidase I	lepB	lep; SPASE I
PA0771		GTP-binding protein Era	era	
PA0776		hypothetical protein		
PA0778		hypothetical protein		
PA0786		probable transporter		
PA0787		hypothetical protein		
PA0790		hypothetical protein		
PA0802		hypothetical protein		
PA0805		hypothetical protein		
PA0808		hypothetical protein	ì	
PA0815		probable transcriptional regulator		
PA0818	9946712	hypothetical protein		
PA0820		hypothetical protein		
PA0822		hypothetical protein	1	
PA0825		hypothetical protein		
PA0826	9946720	hypothetical protein		
PA0829		probable hydrolase	i	
PA0837		peptidyl-prolyl cis-trans isomerase SlyD	slyD	
PA0850		hypothetical protein		
PA0851		hypothetical protein		
PA0853		probable oxidoreductase	1	
PA0857		morphogene protein BolA	bolA	
PA0862		hypothetical protein		
PA0867		hypothetical protein	Ì	
PA0868		conserved hypothetical protein	<u> </u>	yaeJ
PA0869		D-alanyl-D-alanine-endopeptidase	pbpG	
PA0871	0046770	pterin-4-alpha-carbinolamine dehydratase	phhB	
PA0871		hypothetical protein	15	
	0046770	probable ring-cleaving dioxygenase	1	
PA0880		hypothetical protein	;	
PA0894				
PA0900		hypothetical protein	alaS	sya
PA0903	9946804	alanyl-tRNA synthetase	iaiao	

PA0904	9946806 aspartate kinase alpha and beta chain	lysC	ask; akaB
PA0905	9946807 carbon storage regulator	csrA	1
	9946808 probable transcriptional regulator		
PA0906 PA0908	9946810 hypothetical protein	1	
	9946811 hypothetical protein		
PA0909		mgtE	*
PA0913	9946825 hypothetical protein	1	
PA0922	9946831 D-lactate dehydrogenase (fermentative)	ildhA	ldhD
PA0927	994003 I D-lactate derivdrogenase (lettriemative)	cysM	g FAGE 1 had a man unique an area of a man and a man and a man a m
PA0932	9946836 cysteine synthase B	Cysivi	yaiL
PA0937	9946842 conserved hypothetical protein	+	yait
PA0939	9946844 hypothetical protein	purN	1
PA0944	9946849 phosphoribosylaminoimidazole synthetase	ipurM	
PA0945	9946850 phosphoribosylaminoimidazole synthetase	Purivi	
PA0947	9946853 conserved hypothetical protein		helX
PA0953	9946859 probable thioredoxin		Illeix
PA0954	9946860 probable acylphosphatase	- nros	
PA0956	9946862 prolyl-tRNA synthetase	proS	
PA0960	9946867 hypothetical protein		
PA0962	9946869 probable dna-binding stress protein	tolQ	
PA0969	9946876 TolQ protein		
PA0970	9946877 TolR protein	tolR	
PA0971	9946878 TolA protein	tolA	
PA0972	9946879 TolB protein	tolB	T-LoveC
PA0973	9946880 outer membrane protein OprL precursor	oprL	pal excC
PA0976	. 9946884 conserved hypothetical protein		
PA0978	9946886 conserved hypothetical protein		
PA0979	9946887 conserved hypothetical protein		
PA0980	9946888 hypothetical protein		
PA0981	9946889 hypothetical protein		
PA0983	9946891 conserved hypothetical protein		
PA0985	9946893 probable colicin-like toxin		
PA0986	9946894 conserved hypothetical protein	;	
PA0990	9946899 conserved hypothetical protein		
PA0991	9946900 hypothetical protein		
PA0993	9946902 probable pili assembly chaperone		
PA1000	9946909 hypothetical protein		yrki
PA1006	9946916 conserved hypothetical protein	 	yrki .
PA1008	9946918 bacterioferritin comigratory protein	DCD	
PA1010	9946920 dihydrodipicolinate synthase	dapA	incl
PA1012	9946922 conserved hypothetical protein		jyycJ
PA1013	9946923 phosphoribosylaminoimidazole-succinocarb	Oxapuic	
PA1021	9946932 probable enoyl-CoA hydratase/isomerase		
PA1026	9946938 hypothetical protein		
PA1035	9946948 hypothetical protein		
PA1038	9946951 hypothetical protein		ychJ
PA1039	9946952 conserved hypothetical protein	l maled I	успо
PA1049	9946963 pyridoxine 5'-phosphate oxidase	pdxH	nhoC
PA1055	9946969 conserved hypothetical protein		phaC
PA1063	9946978 hypothetical protein		
PA1068	9946983 probable heat shock protein (hsp90 family)		
PA1076	9946992 hypothetical protein		
PA1088	9947004 hypothetical protein		

PA1089	9947005	conserved hypothetical protein		
PA1090	9947006	nypothetical protein		1
PA1095		nypothetical protein		fliS
PA1098	9947015 t	wo-component sensor	fleS	
PA1102	9947019 f	lagellar motor switch protein FliG	fliG	: !
PA1105		flagellar protein FliJ	fliJ	
PA1106	99470231	hypothetical protein		
PA1107	9947025	conserved hypothetical protein		1
PA1114		hypothetical protein		
PA1118		hypothetical protein		į
PA1120	9947039	conserved hypothetical protein	•	yfiN
PA1122		probable peptide deformylase	;	def, pdf, fms
PA1125	9947044	probable cobalamin biosynthetic protein	:	cobB
PA1129	9947049	probable fosfomycin resistance protein	i	
PA1129		hypothetical protein	!	
	9947055	conserved hypothetical protein		yedU
PA1135 PA1138	0047058	probable transcriptional regulator		
	9947036	probable transcriptional regulator	í	
PA1145		hypothetical protein		
PA1149		pyocin S2 immunity protein	imm2	
PA1151	9947075	conserved hypothetical protein	-	
PA1154	9947070	ribonucleoside reductase, small chain	nrdB	
PA1155	9947077	ribonucleoside reductase, small one	nrdA	
PA1156	9947070	probable two-component response regulator		
PA1157	9947000	probable cold-shock protein	;	
PA1159		hypothetical protein	<u>, </u>	
PA1160	9947003	succinyl-diaminopimelate desuccinylase	dapE	
PA1162	9947000	conserved hypothetical protein	1	
PA1164		hypothetical protein		
PA1165		hypothetical protein	;	
PA1167	9947091	hypothetical protein	1	
PA1168	9947092	cytochrome c-type protein NapC	napC	
PA1172	9947090	cytochrome c-type protein NapB precursor	napB	
PA1173 PA1176	0047100	ferredoxin protein NapF	napF	
· · · · · · · · · · · · · · · · · · ·	9947100	periplasmic nitrate reductase protein NapE	inapE	
PA1177	9947101	C4-dicarboxylate transport protein	dctA	
PA1183 PA1193	9947100	hypothetical protein	1	
	0947130	hypothetical protein	i	
PA1203 PA1204	9947130	conserved hypothetical protein	<u> </u>	yieF
PA1204 PA1206	0047133	hypothetical protein	Ť	
	9947133	hypothetical protein	1	
PA1213	0047142	hypothetical protein		
PA1215		hypothetical protein		
PA1216		probable 2-isopropylmalate synthase	i	
PA1217		hypothetical protein	-	
PA1219		probable transcriptional regulator	- 	
PA1223	9947 102	probable NAD(P)H dehydrogenase	i	
PA1224		hypothetical protein	 	
PA1228		hypothetical protein	- 	
PA1230		hypothetical protein	_:	
PA1233	9947162	probable multidrug resistance efflux pump		
PA1237	994/16/	I probable multioring resistance emux pamp	,aprl	
PA1250	994/18	l alkaline proteinase inhibitor Aprl	_::	

PA1261 9947193 probable transcriptional regulator				
PA1269 9947214 hypothetical protein cobC PA1285 9947220 probable transcriptional regulator PA1285 9947231 conserved hypothetical protein yegl. PA1285 99472321 conserved hypothetical protein yegl. PA1298 9947233 probable sigma-70 factor, ECF subfamily yehl. PA1300 9947236 probable sigma-70 factor, ECF subfamily yehl. PA1301 9947244 conserved hypothetical protein yafJ PA1303 9947244 conserved hypothetical protein yafJ PA1303 9947244 conserved hypothetical protein yafJ PA1315 9947252 probable transcriptional regulator yafJ PA1321 9947259 cytochrome o ubiquinol oxidase protein CyoE cyoE PA1323 9947267 probable transcriptional regulator PA1333 9947270 conserved hypothetical protein yegH PA1334 9947280 probable transcriptional regulator yegH PA1344 9947289 probable transcriptional regulator yegH PA1348 9947289 hypothetical protein yegH PA1349 9947290 conserved hypothetical protein yegH PA1340 9947290 conserved hypothetical protein yegH PA1341 9947291 hypothetical protein yegH PA1355 9947291 hypothetical protein yegH PA1365 9947297 hypothetical protein yegH PA1366 9947301 hypothetical protein yegH PA1367 9947301 hypothetical protein yegH PA1368 9947301 hypothetical protein yegH PA1369 9947301 hypothetical protein yegH PA1370 9947311 hypothetical protein yegH PA1371 9947311 yegH yegH	PA1261	9947193 probable transcriptional regulator		
PA1280 9947220 porbable transcriptional regulator porbable signal or porbable signal		9947202 probable transcriptional regulator		
PA1285 9947220 probable transcriptional regulator ycgl.	· -			icobC
PA1295 9947231 conserved hypothetical protein YcgL				
PA1288 9947234 conserved hypothetical protein yohL				
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PA1475	994742811	neme exporter protein CcmA	ccmA	#NAME?
PA1476		neme exporter protein CcmB	ccmB	'cyt10; cycW; helB
PA1477		neme exporter protein CcmC	,ccmC	.pfcyt1 cycZ helC
PA1478 i		hypothetical protein	!	pfcyt2 ccmD cycX helD
PA1480	9947434	cytochrome C-type biogenesis protein CcmF	ccmF	cycK; ccl1
	0047435	cytochrome C biogenesis protein CcmG	ccmG	dsbE
PA1481	0047436	cytochrome C-type biogenesis protein CcmH	ccmH	ccl2 cycL
PA1482		hypothetical protein	-	
PA1488		hypothetical protein		
PA1489		hypothetical protein	<u> </u>	
PA1492			!	
PA1496		probable potassium channel	 	A CONTRACTOR OF THE PARTY AND ADMINISTRATION OF THE PARTY
PA1504		probable transcriptional regulator		
PA1508		hypothetical protein	 	
PA1509		hypothetical protein	 	L.T
PA1514		conserved hypothetical protein		ybbT
PA1517	9947474	conserved hypothetical protein		
PA1518	9947475	conserved hypothetical protein	 	
PA1526	9947484	probable transcriptional regulator	<u> </u>	
PA1528		cell division protein ZipA	zipA	
PA1529	9947487	DNA ligase	lig	dnaL ligA
PA1532	9947490	DNA polymerase subunits gamma and tau	dnaX	
PA1533	9947491	conserved hypothetical protein	<u> </u>	
PA1535	9947494	probable acyl-CoA dehydrogenase		
PA1539		hypothetical protein		
PA1540	9947499	conserved hypothetical protein		
PA1541	9947500	probable drug efflux transporter	<u> </u>	
PA1548	9947508	conserved hypothetical protein		fixS
PA1551		probable ferredoxin		fixG
PA1555		probable cytochrome c	(fixP ccoP
PA1558		hypothetical protein	i	
PA1559		hypothetical protein	1	
PA1560		hypothetical protein	1	
PA1564	9947526	conserved hypothetical protein	1	
PA1568	9947530	conserved hypothetical protein		
PA1571	9947533	hypothetical protein	1	
PA1581	9947544	succinate dehydrogenase (C subunit)	sdhC	cybA
PA1582	9947545	succinate dehydrogenase (D subunit)	sdhD	
PA1583	9947546	succinate dehydrogenase (A subunit)	sdhA	
	9947547	succinate dehydrogenase (B subunit)	sdhB	
PA1584	00/7550	lipoamide dehydrogenase-glc	lpdG	lpdA
PA1587	0047550	succinyl-CoA synthetase beta chain	sucC	
PA1588	0047553	succinyl-CoA synthetase beta chain succinyl-CoA synthetase alpha chain	sucD	
PA1589	994/553	hypothetical protein	1	1
PA1591			†	
PA1592		hypothetical protein	· · · · · · · · · · · · · · · · · · ·	
PA1593		hypothetical protein		
PA1594		hypothetical protein	 	
PA1595	9947559	hypothetical protein	fabA	
PA1610		beta-hydroxydecanoyl-ACP dehydrase	Hann	ybdB
PA1618	9947584	conserved hypothetical protein	- 	youb
PA1619	9947585	probable transcriptional regulator		
PA1622	9947589	probable hydrolase	<u>:</u>	
PA1623	9947590	conserved hypothetical protein		<u> </u>

		· · · · · · · · · · · · · · · · · · ·	1
PA1624	9947591 hypothetical protein	· 	
PA1630	9947597 probable transcriptional regulator	kdpF	
PA1632	9947600 KdpF protein		atkC
PA1635	9947603 potassium-transporting ATPase, C chain	ikdpC	
PA1638	9947606 conserved hypothetical protein	<u> </u>	yneH
PA1641	9947610 hypothetical protein	<u>; </u>	
PA1645	9947614 hypothetical protein	<u>:</u>	<u>i</u>
PA1657 !	9947627 conserved hypothetical protein	,	
PA1664	9947635 hypothetical protein	1	
PA1666	9947637 hypothetical protein		
PA1673	9947645 hypothetical protein	<u> </u>	
PA1674	9947646 GTP cyclohydrolase I precursor	folE2	
PA1675	9947647 conserved hypothetical protein	<u> </u>	
PA1676	9947648 hypothetical protein	<u>i</u>	
PA1687	9947660 spermidine synthase	speE	
PA1690	9947663 translocation protein in type III secretion	pscU	
PA1691	9947664 translocation protein in type III secretion	pscT	
PA1696	9947669 translocation protein in type III secretion	pscO	
PA1698	9947672 outer membrane protein PopN	popN	
PA1090 PA1701	9947675 conserved hypothetical protein in type III secr	e	pcr3
PA1701	9947676 conserved hypothetical protein in type III secr	e	pcr4
PA1702 PA1705	9947679 regulator in type III secretion	pcrG	
PA1705	9947684 exoenzyme S synthesis protein C precursor	exsC	
	9947685 hypothetical protein		
PA1711	9947693 type III export protein PscE	pscE	
PA1718	9947694 type III export protein PscF	pscF	
PA1719	9947695 type III export protein PscG	pscG	
PA1720	9947697 type III export protein Pscl	psci	
PA1722	9947708 conserved hypothetical protein		
PA1732	9947709 conserved hypothetical protein		
PA1733	9947720 hypothetical protein		
PA1743	9947722 hypothetical protein		
PA1745	9947725 hypothetical protein	_ 	
PA1747	9947728 phospho-2-dehydro-3-deoxyheptonate aldola	ise	
PA1750	9947735 homoserine kinase	thrH	
PA1757	9947747 hypothetical protein		
PA1768	9947747 hypothetical protein 9947752 probable methyltransferase	- 	menG
PA1772	9947757 outer membrane protein OprF precursor	oprF	
PA1777	9947760 assimilatory nitrite reductase small subunit	nirD	nasE
PA1780	9947760 assimilatory filtrite reductase sittali subutiti	nasA	nasT
PA1783	9947764 nitrate transporter	11.00.	nasT
PA1785	9947766 conserved hypothetical protein	acnB	
PA1787	9947768 aconitate hydratase 2	-lacing	
PA1790	9947772 hypothetical protein	<u> </u>	ybbF
PA1792	9947774 conserved hypothetical protein	glnS	<u> </u>
PA1794	9947776 glutaminyl-tRNA synthetase	cysS	
PA1795	9947777 cysteinyl-tRNA synthetase		
PA1796	9947778 5,10-methylene-tetrahydrofolate dehydroger	lon	capR deg muc lopA
PA1803	9947786 Lon protease	lon	Capit deg muciopit
PA1815	9947800 ribonuclease H	rnhA	
PA1816	9947801 DNA polymerase III, epsilon chain	dnaQ	mutD
PA1817	9947802 hypothetical protein		
PA1820	9947805 sodium/proton antiporter NhaB	nhaB	

PA1825	9947811 hypothetical protein		
PA1830	9947816 hypothetical protein	<u> </u>)
PA1835	9947821 hypothetical protein	<u> </u>	į
PA1837	9947823 hypothetical protein	<u> </u>	
PA1840	9947827 hypothetical protein		<u> </u>
PA1842	9947829 hypothetical protein	1	
PA1845	9947832 hypothetical protein		
PA1847	9947835 conserved hypothetical protein		yhgi
PA1852	9947840 hypothetical protein	}	
PA1855	9947843 hypothetical protein	T	
PA1859	9947848 probable transcriptional regulator		
	9947851 molybdenum transport protein ModB	modB	
PA1862	9947857 hypothetical protein		xphA
PA1867	9947859 probable acyl carrier protein		
PA1869	9947862 hypothetical protein		
PA1872	9947873 probable transporter	 	
PA1882	9947874 probable NADH-ubiquinone/plastoquinone ox	id	
PA1883	9947875 probable transcriptional regulator		
PA1884	9947876 conserved hypothetical protein	†	
PA1885	9947884 hypothetical protein	†	
PA1892	9947886 hypothetical protein		
PA1894	9947887 hypothetical protein		
PA1895	9947887 Inypothetical protein	1	
PA1896	9947888 hypothetical protein		
PA1897	9947889 hypothetical protein 9947892 probable phenazine biosynthesis protein	-	phzA2
PA1899	9947892 probable phenazine biosynthesis protein	-	phzB2
PA1900	9947893 probable phenazine biosynthesis protein 9950429 probable pyridoxamine 5'-phosphate oxidase	- 	phzG2
PA1905	9947904 probable transmembrane sensor	.	
PA1911	9947905 probable sigma-70 factor, ECF subfamily	-	
PA1912	9947907 conserved hypothetical protein		hvn
PA1914	9947910 hypothetical protein		
PA1917	9947918 hypothetical protein	<u> </u>	
PA1924	9947919 hypothetical protein		
PA1925	9947923 ribosomal protein alanine acetyltransferase	rimJ	
PA1928	9947924 hypothetical protein		
PA1929	9947932 hypothetical protein		
PA1936	9947933 conserved hypothetical protein	1	
PA1937	9947934 conserved hypothetical protein	- 	
PA1938	9947935 hypothetical protein		
PA1939	9947949 hypothetical protein	_	
PA1951	9947950 hypothetical protein		
PA1952	9947953 hypothetical protein		
PA1955	9947954 hypothetical protein		
PA1956	9947954 hypothetical protein 9947960 conserved hypothetical protein	- i	
PA1962			
PA1963	9947962 hypothetical protein	+	
PA1965	9947964 hypothetical protein	-i	
PA1967	9947966 hypothetical protein	- 	
PA1968	9947967 hypothetical protein		
PA1974	9947974 hypothetical protein		agmR
PA1978	9947978 probable transcriptional regulator		laginix
PA1980	9947980 probable two-component response regulator	n Anga ^	,
PA1985	9947986 pyrroloquinoline quinone biosynthesis protei	п урчч	

PA1986	9947987	pyrroloquinoline quinone biosynthesis protein 🛭	pqqB	
PA1988	9947989	pyrroloquinoline quinone biosynthesis protein 🗓	pqqD	
PA1994		nypothetical protein		
PA1995		nypothetical protein		
PA1996	9947998 r	peptidyl-prolyl cis-trans isomerase C1	ppiC1	
PA2001	9948003	acetyl-CoA acetyltransferase	atoB	
PA2001	9948004	conserved hypothetical protein		atoE
PA2002 :	9948010	maleylacetoacetate isomerase	maiA	
· · · · · · · · · · · · · · · · · · ·	0048013	probable transcriptional regulator		
PA2010	0048016	probable enoyl-CoA hydratase/isomerase		ImenB
PA2013	00480101	probable acyl-CoA dehydrogenase		
PA2015	0049020	probable transcriptional regulator		
PA2016		hypothetical protein	· · · · · · · · · · · · · · · · · · ·	
PA2017		hypothetical protein		
PA2021	9946023[1	conserved hypothetical protein		yfeH
PA2026		hypothetical protein	'	
PA2029		hypothetical protein		
PA2031		hypothetical protein		
PA2034		hypothetical protein		
PA2037	9946043	probable transporter (membrane subunit)		ygjU
PA2042	9946046	probable transmembrane sensor		
PA2051		cyanate lyase	cynS	
PA2052	0049069	probable permease of ABC transporter		
PA2060	9946006	probable pyridoxal-phosphate dependent enzy		
PA2062	9946071	hypothetical protein		
PA2066	9946075	elongation factor G	fusA2	
PA2071 PA2073	0048083	probable transporter (membrane subunit)		
PA2073	9948084	hypothetical protein		
PA2075		hypothetical protein		
PA2080		hypothetical protein		
PA2088	9948100	hypothetical protein		
PA2090	9948102	hypothetical protein		
PA2092	9948104	probable MFS transporter		
PA2095	9948108	hypothetical protein		
PA2097	9948110	probable flavin-binding monooxygenase		
PA2101	9948114	conserved hypothetical protein		
PA2103	9948117	probable molybdopterin biosynthesis protein N	4	moeB
PA2105	9948119	probable acetyltransferase		
PA2107	9948121	hypothetical protein		
PA2110		hypothetical protein		
PA2118	9948133	O6-methylguanine-DNA methyltransferase	ada	
PA2119	9948134	alcohol dehydrogenase (Zn-dependent)		adh
PA2120	9948135	hypothetical protein		
PA2123	9948138	probable transcriptional regulator		
PA2126	9948142	conserved hypothetical protein		
PA2131	9948147	hypothetical protein		
PA2136	9948153	hypothetical protein		
PA2142	9948159	probable short-chain dehydrogenase		yhxC
PA2143		hypothetical protein		
PA2146	9948164	conserved hypothetical protein	1	yciG
PA2149	9948167	hypothetical protein	1	
PA2157		hypothetical protein		
11 12101	1 33.0.110	7		

PA2161	9948180 hypothetical protein)	
PA2166	9948186 hypothetical protein		
PA2167	9948187 hypothetical protein	Į.	
PA2170	9948190 hypothetical protein		
PA2171	9948191 hypothetical protein		
PA2174	9948194 hypothetical protein	1	
PA2175	9948195 hypothetical protein		
PA2182	9948203 hypothetical protein	;	
PA2183	9948204 hypothetical protein		;
PA2184	9948205 conserved hypothetical protein		yciE
PA2185	9948206 hypothetical protein		
PA2186	9948207 hypothetical protein		1
PA2187	9948208 hypothetical protein		
PA2190	9948211 conserved hypothetical protein		
	9948214 conserved hypothetical protein		
PA2192	9948218 probable transcriptional regulator	or I	
PA2196	9948219 conserved hypothetical protein		ycnB
PA2197	9948228 hypothetical protein		
PA2205	9948230 hypothetical protein		
PA2207 PA2211	9948234 conserved hypothetical protein		
PA2211	9948238 probable MFS transporter		
PA2214 PA2219	9948243 membrane protein OpdE	opdE	
PA2219 PA2220	9948244 probable transcriptional regulate		oprR
PA2220 PA2221	9948245 conserved hypothetical protein		
PA2221 PA2222	9948247 hypothetical protein		
PA2222 PA2223	9948248 hypothetical protein		
PA2223 PA2224	9948249 hypothetical protein		
PA2224	9948250 hypothetical protein		
PA2226	9948251 hypothetical protein		
PA2227	9948252 probable transcriptional regulate	or ·	
PA2228	9948253 hypothetical protein		
PA2229	9948254 conserved hypothetical protein		yiiM
PA2234	9948259 probable exopolysaccharide tra	nsporter	
PA2242	9948268 hypothetical protein		
PA2245	9948271 hypothetical protein		
PA2251	9948278 hypothetical protein		
PA2253	9948280 L-asparaginase I	ansA	
PA2257	9948284 pyoverdine biosynthesis proteir	PvcD pvcD	
PA2258	9948285 transcriptional regulator PtxR	ptxR	
PA2260	9948288 hypothetical protein	·	
PA2280	9948309 conserved hypothetical protein		arsH
PA2282	9948312 hypothetical protein		
PA2284	9948314 hypothetical protein		!
PA2292	9948323 hypothetical protein		
PA2293	9948324 hypothetical protein		
PA2294	9948325 probable ATP-binding compon	ent of ABC trans	
PA2295	9948326 probable permease of ABC tra	nsporter	
PA2297	9948328 probable ferredoxin		
PA2298	9948329 probable oxidoreductase		
PA2303	9948335 hypothetical protein		
PA2311	9948344 hypothetical protein		!
PA2316	9948349 probable transcriptional regula	tor	i i
1742010	1 00.00.01		

PA2329 ;	9948364 probable ATP-binding component of ABC t	rans	
PA2331	9948366 hypothetical protein		2
PA2336	9948371 hypothetical protein		
PA2338	9948374 probable binding protein component of ABO	C m	mtlE
PA2343	9948379 xylulose kinase	·mtlY	*
PA2347	9948384 hypothetical protein	<u> </u>	;
PA2349	9948386 conserved hypothetical protein		<u> </u>
PA2351	9948388 probable permease of ABC transporter		1
PA2365	9948403 conserved hypothetical protein	<u>;</u>	
PA2367	9948406 hypothetical protein	į	
PA2368	9948407 hypothetical protein		
PA2370	9948409 hypothetical protein		
PA2372	9948411 hypothetical protein	[
PA2375	9948414 hypothetical protein		
PA2383	9948423 probable transcriptional regulator	!	
PA2391	9948432 probable outer membrane protein		
PA2391	9948449 hypothetical protein		
PA2406	9948450 hypothetical protein		
PA2400 PA2411	9948455 probable thioesterase	1	
PA2411 PA2412	9948456 conserved hypothetical protein	<u> </u>	
PA2412 PA2418	9948463 hypothetical protein	<u>. j </u>	
	9948467 hypothetical protein		
PA2422	9948473 hypothetical protein		
PA2427	9948474 hypothetical protein		
PA2428	9948475 hypothetical protein	<u>!</u>	
PA2429	9948480 hypothetical protein		
PA2434	9948482 hypothetical protein	i	
PA2436	9948488 hypothetical protein		
PA2441	9948489 glycine cleavage system protein T2	gcvT2	
PA2442 PA2446	9948494 glycine cleavage system protein H2	gcvH2	
PA2446 PA2451	9948499 hypothetical protein		
PA2451	9948502 hypothetical protein	i	
	9948504 hypothetical protein	1	
PA2455	9948505 hypothetical protein	ĺ	
PA2456 PA2459	9948508 hypothetical protein	<u> </u>	
PA2459 PA2460	9948509 hypothetical protein	1	
PA2461	9948510 hypothetical protein		
PA2464	9948514 hypothetical protein		-
PA2467	9948517 probable transmembrane sensor		
PA2469	9948519 probable transcriptional regulator		
	9948524 probable glutathione S-transferase	<u> </u>	
PA2473	9948525 hypothetical protein	<u>-</u>	
PA2474	9948526 probable cytochrome P450		
PA2475	9948537 hypothetical protein		
PA2485	9948539 hypothetical protein		
PA2487	9948542 conserved hypothetical protein		ydbB
PA2490	9948543 probable oxidoreductase	- i	
PA2491	9948544 transcriptional regulator MexT	mexT	
PA2492			
PA2496	9948549 hypothetical protein		cynX
PA2500	9948553 probable MFS transporter		
PA2501	9948554 hypothetical protein	· · · · · · · · · · · · · · · · · · ·	
PA2504	9948557 hypothetical protein	i	

PA2507	9948561 _{[C}	according the aloxygoness	catA		;
PA2515	9948569 c	is-1,2-dihydroxycyclohexa-3,4-diene carboxyl	axylL	\$	
PA2517	9948571 to	oluate 1.2-dioxygenase beta subunit	xylY		· i
PA2521	9948576 F	RND divalent metal cation efflux membrane fu	czcB		
PA2536	9948593 p	probable phosphatidate cytidylyltransferase		jynbB	
PA2538		nypothetical protein		:	
PA2539	9948596	conserved hypothetical protein	,	ynbD	
PA2539	9948602 h	nypothetical protein		1	
	0048608	conserved hypothetical protein		lygjT	
PA2549	0048610	probable transcriptional regulator			
PA2551	0049611	probable acyl-CoA dehydrogenase		acdB	
PA2552	0049612 r	probable acyl-CoA thiolase		!	
PA2553	0048613	probable short-chain dehydrogenase			\neg
PA2554	00/19630	probable transcriptional regulator			
PA2577	9940039[CDP-diacylglycerolglycerol-3-phosphate 3-ph	pasA		
PA2584	9940047	probable transcriptional regulator	[]		
PA2591	9940033	nypothetical protein			
PA2602	994000711	conserved hypothetical protein		yheN	
PA2605	99486701	conserved hypothetical protein	 	yheM	
PA2606	994867110	conserved hypothetical protein	,		
PA2607	99486721	conserved hypothetical protein		yccK	
PA2608	9948673	seryl-tRNA synthetase	serS		
PA2612	9948677	periplasmic chaperone LoIA	lolA		
PA2614	9948680	periplasmic chaperone LoiA	ftsK		
PA2615	9948681	cell division protein FtsK leucyl/phenylalanyl-tRNA-protein transferase	aat		
PA2617	9948683	initiation factor	infA		
PA2619	9948683	conserved hypothetical protein			
PA2621	9948667	tRNA methyltransferase	trmU	asuE	
PA2626		adenylosuccinate lyase	purB		
PA2629	9948696	NADH dehydrogenase I chain B	nuoB		
PA2638	9948706	NADH dehydrogenase I chain F	nuoF		
PA2641	9946709	NADH dehydrogenase I chain J	nuoJ		
PA2645	9940714	NADH dehydrogenase I chain K	nuoK		
PA2646		hypothetical protein			
PA2658		hypothetical protein	 	}	
PA2663	9940734	probable 6-pyruvoyl tetrahydrobiopterin syntha	a a	ptpS	
PA2666	0048738	conserved hypothetical protein	1		
PA2667		hypothetical protein	1		
PA2668	0049744	probable type II secretion system protein	1	hplV	
PA2673	9940744	probable type II secretion system protein	 	hplU	
PA2674	9946745	probable type II secretion system protein	 	hplT	
PA2675	9946740	probable permease of ABC-2 transporter	-		
PA2678	9940749	probable transcriptional regulator			
PA2681	9946755	probable transcriptional regulators probable serine/threonine dehydratase, degra	ad	tdcB	
PA2683	9946755	hypothetical protein	1		
PA2689	9948782	probable transposase	 		
PA2690		probable thioredoxin	 		
PA2694		hypothetical protein	1		
PA2697					
PA2703		hypothetical protein	 		
PA2706	9948780	hypothetical protein	1		
PA2715	9948790	probable ferredoxin	-		
PA2719	i 9948795	hypothetical protein			

PA2720	9948796 hypothetical protein		<u> </u>
PA2721	9948797 hypothetical protein		
PA2722	9948798 hypothetical protein	! !	
PA2723	9948799 hypothetical protein		
PA2726	9948802 probable radical activating enzyme		
	9948807 hypothetical protein		
PA2730	9948808 hypothetical protein		
PA2731	9948810 conserved hypothetical protein	1	1
PA2733	9948811 hypothetical protein		
PA2734	9948811 hypothetical protein		
PA2736	9948814 Inypothetical protein		
PA2737	9948815 conserved hypothetical protein	himA	1
PA2738	9948816 integration host factor, alpha subunit	pheT	
PA2739	9948817 phenylalanyl-tRNA synthetase, beta subunit	pheS	
PA2740	9948818 phenylalanyl-tRNA synthetase, alpha-subunit	rpiT	
PA2741	9948819 50S ribosomal protein L20	rpml	
PA2742	9948820 50S ribosomal protein L35	infC	
PA2743	9948821 translation initiation factor IF-3	thrS	
PA2744	9948822 threonyl-tRNA synthetase		
PA2749	9948828 DNA-specific endonuclease I	endA	
PA2753	9948832 hypothetical protein		
PA2756	9948835 hypothetical protein	ļ 	
PA2759	9948839 hypothetical protein	<u> </u>	
PA2762	9948842 hypothetical protein	<u> </u>	
PA2763	9948843 hypothetical protein		
PA2767	9948847 probable enoyl-CoA hydratase/isomerase	<u> </u>	
PA2768	9948848 hypothetical protein		1
PA2769	9948849 hypothetical protein		
PA2774	9948855 hypothetical protein		
PA2775	9948856 hypothetical protein		
PA2780	9948861 hypothetical protein		
PA2781	9948862 hypothetical protein		
PA2782	9948863 hypothetical protein	<u>. J </u>	
PA2784	9948866 hypothetical protein	1	
PA2785	9948867 conserved hypothetical protein		
PA2786	9948868 hypothetical protein		
PA2792	9948874 hypothetical protein	į.	
PA2794	9948877 hypothetical protein		
PA2797	9948880 hypothetical protein		
	9948882 hypothetical protein		
PA2799	9948883 conserved hypothetical protein		vacJ
PA2800	9948886 hypothetical protein		
PA2803	9948888 hypothetical protein	1	
PA2805	9948891 hypothetical protein		
PA2807	9948892 hypothetical protein	1	
PA2808	9948895 probable permease of ABC-2 transporter		yadH
PA2811	9948090 probable permease of ADO-2 demoporter	- 	
PA2818	9948902 hypothetical protein	- i	
PA2819	9948903 hypothetical protein		yeaA
PA2827	9948912 conserved hypothetical protein		
PA2829	9948914 hypothetical protein		
PA2831	9948917 conserved hypothetical protein	Itom	
PA2832	9948918 thiopurine methyltransferase	tpm	ygiD .
PA2839	9948925 conserved hypothetical protein	:	

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		1

PA2843	9948930 probable aldolase	: 	
PA2845	9948932 hypothetical protein		
PA2851	9948938 translation elongation factor P	efp	:
PA2852	9948939 hypothetical protein	•	1
PA2853	9948941 outer membrane lipoprotein Oprl precurso	or oprl	
PA2854	9948942 conserved hypothetical protein		erfK
	9948947 transcription elongation factor GreB	greB	;
PA2859	9948951 lipase modulator protein	lipH	
PA2863	9948957 hypothetical protein	!	· · · · · · · · · · · · · · · · · · ·
PA2868	9948963 hypothetical protein		
PA2874	9948966 orotidine 5'-phosphate decarboxylase	ругЕ	
PA2876	9948967 probable transcriptional regulator	<u> </u>	
PA2877	9948969 probable transcriptional regulator		hpkR
PA2879	9948969 probable transcriptional regulator		
PA2883	9948973 hypothetical protein		
PA2894	9948985 hypothetical protein		
PA2898	9948990 hypothetical protein		
PA2901	9948993 hypothetical protein	- 1	yebN
PA2910	9949003 conserved hypothetical protein		Jes.v
PA2915	9949008 hypothetical protein	<u> </u>	
PA2916	9949010 hypothetical protein		
PA2922	9949016 probable hydrolase		
PA2928	9949023 hypothetical protein		
PA2935	9949030 hypothetical protein		
PA2936	9949031 hypothetical protein		
PA2937	9949033 hypothetical protein		
PA2940	9949036 probable acyl-CoA thiolase		
PA2949	9949046 probable lipase	nit etfA	
PA2951	9949048 electron transfer flavoprotein alpha-subu	it etfB	
PA2952	9949049 electron transfer flavoprotein beta-subun		
PA2953	9949050 electron transfer flavoprotein-ubiquinone	pilZ	
PA2960	9949058 type 4 fimbrial biogenesis protein PilZ	holB	
PA2961	9949059 DNA polymerase III, delta prime subunit	tmk	
PA2962	9949060 thymidylate kinase	unk	yceG
PA2963	9949061 conserved hypothetical protein		yced
PA2966	9949064 acyl carrier protein	acpP	
PA2967	9949065 3-oxoacyl-[acyl-carrier-protein] reductase	fabG	
PA2968	9949066 malonyl-CoA-[acyl-carrier-protein] transa	cylaserabD	
PA2970	9949069 50S ribosomal protein L32	rpmF	11000
PA2971	9949070 conserved hypothetical protein		yceD
PA2975	9949074 ribosomal large subunit pseudouridine s	yntnas riuC	yceC
PA2977	9949076 UDP-N-acetylpyruvoylglucosamine redu	ctase murb	
PA2978	9949077 phosphotyrosine protein phosphatase	ptpA	
PA2979	9949078 3-deoxy-manno-octulosonate cytidylyltra	nsterakdsB	
PA2980	9949079 conserved hypothetical protein		ycaR
PA2981	9949080 tetraacyldisaccharide 4*-kinase	lpxK	
PA2982	9949081 conserved hypothetical protein		
PA2983	9949082 probable tolQ-type transport protein		
PA2985	9949085 hypothetical protein		
PA2986	9949086 conserved hypothetical protein		
PA2987	9949087 probable ATP-binding component of AB	C trans	ycfV
PA2988	9949088 conserved hypothetical protein	ţ	
PA2989	9949089 hypothetical protein	;	
1 V5 303			

PA2991	9949091 soluble pyridine nucleotide transhydrogenase	isth	
PA2991	9949092 hypothetical protein	-	
	9949096 Na+-translocating NADH:uniquinone oxidored	dignarD	
PA2996	9949102 probable glyceraldehyde-3-phosphate dehydr	d	1
PA3001	9949105 probable nucleoside phosphorylase	1	
PA3004	9949111 hypothetical protein	<u>i </u>	
PA3009	9949111 hypothetical protein	topA	
PA3011	9949113 DNA topoisomerase I	Hopri	
PA3012	9949114 hypothetical protein		
PA3017	9949120 conserved hypothetical protein		
PA3021	9949124 hypothetical protein		
PA3022	9949125 hypothetical protein		
PA3024	9949127 probable carbohydrate kinase		mob A
PA3030	9949134 probable molybdopterin-guanine dinucleotide	<u> </u>	mobA
PA3033	9949137 hypothetical protein		
PA3036	9949140 hypothetical protein		
PA3040	9949145 conserved hypothetical protein		yqjD
PA3041	9949146 hypothetical protein		yqjE
PA3042	9949147 hypothetical protein		
PA3046	9949151 conserved hypothetical protein		yggL
PA3049	9949155 ribosome modulation factor	rmf	
PA3051	9949157 hypothetical protein	.	
PA3067	9949174 probable transcriptional regulator		
PA3081	9949189 conserved hypothetical protein		·
PA3085	9949193 hypothetical protein		·
PA3088	9949197 conserved hypothetical protein		yfjB
PA3089	9949198 hypothetical protein		
PA3093	9949202 hypothetical protein		
PA3095	9949205 general secretion pathway protein M	xcpZ	
PA3096	9949206 general secretion pathway protein L	xcpY	
PA3100	9949210 general secretion pathway protein H	xcpU	pddB
PA3103	9949213 general secretion pathway protein E	xcpR	
PA3103	9949221 hypothetical protein		
PA3112	9949223 acetyl-CoA carboxylase beta subunit	accD	dedB
PA3117	9949229 aspartate semialdehyde dehydrogenase	asd	•
PA3123	9949235 conserved hypothetical protein		· ·
	9949254 hypothetical protein		
PA3140	9949256 hypothetical protein		
PA3142	9949258 hypothetical protein		· · · · · · · · · · · · · · · · · · ·
PA3144	9949259 glycosyltransferase WbpL	wbpL	
PA3145	9949260 probable NAD-dependent epimerase/dehyd		
PA3146	9949261 probable glycosyl transferase WbpJ	wbpJ	
PA3147	9949261 probable glycosyl transfer ase vvopo 9949262 probable UDP-N-acetylglucosamine 2-epim		
PA3148	9949262 probable ODP-N-acetylgideosaminic 2-cpini	wbpH	
PA3149	9949263 probable glycosyltransferase WbpH	wbpG	
PA3150	9949264 LPS biosynthesis protein WbpG		
PA3151	9949266 imidazoleglycerol-phosphate synthase, cycl	hisH2	
PA3152	9949267 glutamine amidotransferase	WZX	wbpF, rfbX
PA3153	9949268 O-antigen translocase		rfc
PA3154	9949269 B-band O-antigen polymerase	wzy	110
PA3155	9949270 probable aminotransferase WbpE	wbpE	
PA3156	9949271 probable acetyltransferase WbpD	wbpD	
PA3157	9949272 probable acetyltransferase		wbpC
PA3158	9949273 probable oxidoreductase WpbB	wbpB	

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PA3159		probable UDP-glucose/GDP-mannose dehydro	WODA	
PA3160		o dilligori oridiri lorigari logulare.	WZZ	cld, rol
PA3161		ntegration host factor beta subunit	himD	
PA3162 ;		30S ribosomal protein S1	rpsA	
PA3163	9949279	cytidylate kinase	cmk	
PA3167 :		3-phosphoserine aminotransferase	serC	:
PA3168	9949285	DNA gyrase subunit A	дугА	1
PA3171	9949288	3-demethylubiquinone-9 3-methyltransferase	ubiG	
PA3178	9949296	hypothetical protein		
PA3181	9949299	2-keto-3-deoxy-6-phosphogluconate aldolase		edaA
PA3185	9949303	hypothetical protein		
PA3195	9949314	glyceraldehyde 3-phosphate dehydrogenase	gapA	
PA3202	9949322	conserved hypothetical protein		ycil
PA3203		hypothetical protein		
PA3207		hypothetical protein		
PA3211	9949331	probable permease of ABC transporter		
PA3220	9949341	probable transcriptional regulator		
PA3227	9949348	peptidyl-prolyl cis-trans isomerase A	ppiA	сурН
PA3230	9949352	conserved hypothetical protein		
PA3232		probable nuclease		
PA3237		hypothetical protein		
PA3242	9949365	probable lauroyl acyltransferase		htrB
PA3242	9949368	cell division topological specificity factor MinE	minE	
PA3245	9949300	pseudouridine synthase RluA	rluA	yabO
PA3249		probable transcriptional regulator	i	
PA3249		hypothetical protein	i	
PA3260	9949379	probable transcriptional regulator	İ	
PA3266	9949304	cold acclimation protein B	сарВ	cspA
PA3273	0040308	hypothetical protein	1	
PA3273		hypothetical protein		
PA3274 PA3275	9949399	conserved hypothetical protein	<u> </u>	ynfA
PA3278		hypothetical protein	Ì	
PA3276	9949404	outer membrane porin OprO precursor	oprO	
PA3281	9949400	hypothetical protein		
PA3287	0040414	conserved hypothetical protein	 	
PA3288	0040415	hypothetical protein	†	
PA3289	9949415	hypothetical protein		
		hypothetical protein	 	
PA3291		hypothetical protein	i	
PA3292		hypothetical protein	 	
PA3298	9949420	conserved hypothetical protein	 	
PA3302		conserved hypothetical protein	 	
PA3309	0040444	probable 3-hydroxyisobutyrate dehydrogenase	 	1:
PA3312	0040441	probable ATP-binding component of ABC tran	15	
PA3314	00404443	probable permease of ABC transporter	T	
PA3315		hypothetical protein	1	
PA3317			 	
PA3318		hypothetical protein	1	
PA3320	9949450	hypothetical protein	 	
PA3326	9949457	probable Clp-family ATP-dependent protease	 	
PA3330	9949461	probable short chain dehydrogenase	} -	
PA3332	9949463	conserved hypothetical protein	<u> </u>	
PA3334	9949465	probable acyl carrier protein	·	

PA3338		hypothetical protein		
PA3341 !		probable transcriptional regulator		
PA3347	9949480	hypothetical protein		
PA3348		probable chemotaxis protein methyltransferase	<u> </u>	cheR1
PA3351	9949484	hypothetical protein		flgM
PA3353	9949486	hypothetical protein	·	-
PA3354	9949487	hypothetical protein		
PA3360	9949494	probable secretion protein	·	
PA3367	9949502	hypothetical protein	!	ydcA
PA3368	9949503	probable acetyltransferase		<u>i</u>
PA3370		hypothetical protein		
PA3371		hypothetical protein		
PA3380		conserved hypothetical protein		phnG
PA3384	9949519	ATP-binding component of ABC phosphonate	phnC	
PA3390		hypothetical protein		
PA3395		NosY protein	nosY	
PA3395 PA3396		NosL protein	nosL	
PA3396 PA3397	9949532	ferredoxin-NADP+ reductase	fpr	
PA3397		hypothetical protein		
	0040545	heme acquisition protein HasAp	hasAp	
PA3407		conserved hypothetical protein		vebG
PA3413		hypothetical protein	<u> </u>	
PA3414	9949552	probable pyruvate dehydrogenase E1 compor		
PA3416	9949554	broable pyruvate deriyurogenase E r compor	}	
PA3432	9949572	hypothetical protein	 	ywbl
PA3433		probable transcriptional regulator		7,7,7,
PA3434	9949574	probable transposase	1	mioC
PA3435	9949575	conserved hypothetical protein	folE1	
PA3438	9949578	GTP cyclohydrolase I precursor	folX	
PA3439	9949579	d-erythro-7,8-dihydroneopterin triphosphate	1012	ssuC ycbM
PA3443	9949584	probable permease of ABC transporter	 	ssuD
PA3444		conserved hypothetical protein	!	- 10002
PA3445		conserved hypothetical protein		ssuE
PA3446		conserved hypothetical protein		IsfA
PA3450		probable antioxidant protein	 	ISIA
PA3451		hypothetical protein	 	
PA3460		probable acetyltransferase		
PA3470		hypothetical protein	 	
PA3472		hypothetical protein)	
PA3477		transcriptional regulator RhIR	rhIR	
PA3482		methionyl-tRNA synthetase	metG	
PA3488	9949634	hypothetical protein	 	
PA3489	9949635	conserved hypothetical protein	<u> </u>	rnfA
PA3492		conserved hypothetical protein		rnfD
PA3494		conserved hypothetical protein		rnfE
PA3495		endonuclease III	nth	
PA3496		hypothetical protein		
PA3501	9949647	hypothetical protein		
PA3502		hypothetical protein	<u> </u>	
PA3505	9949652	hypothetical protein	<u> </u>	
PA3512	9949659	probable permease of ABC transporter	i	Į .
PA3519		hypothetical protein	:	
PA3520		hypothetical protein		
・トレシスク	1 0040000	1 Langaran b. a.a		

PA3523	9949671 p	probable RND efflux membrane fusion protein		
PA3528	9949677 r	ibonuclease Ti	rnt	
PA3530	9949679	conserved hypothetical protein		bfd
PA3533		conserved hypothetical protein		ydhD
PA3542	9949693	alginate biosynthesis protein Alg44		alg44
PA3550	9949702	alginate o-acetyltransferase AlgF	algF	
PA3558		nypothetical protein		1
PA3566	9949719	conserved hypothetical protein		ıycnE
PA3570	9949724 г	nethylmalonate-semialdehyde dehydrogenase	mmsA	
PA3572	9949726	nypothetical protein		
PA3575		hypothetical protein		
PA3578		conserved hypothetical protein		
PA3589	9949744	probable acyl-CoA thiolase		
PA3600	9949756	conserved hypothetical protein		rpl36
PA3601	9949757	conserved hypothetical protein		ykgM
PA3605		hypothetical protein		
PA3606		conserved hypothetical protein		yfiP ·
1	9949766	polyamine transport protein PotC	potC	
PA3609	9949768	hypothetical protein		
PA3611 PA3612	0040760	conserved hypothetical protein		уреВ
		conserved hypothetical protein		recX
PA3616		RecA protein	recA	
PA3617	9949775	conserved hypothetical protein		ygbB
PA3627		conserved hypothetical protein		yedF
PA3632		conserved hypothetical protein		ygbP
PA3633	99497921	conserved hypothetical protein		ybgQ
PA3634	9949793		eno	
PA3635	9949794	2-dehydro-3-deoxyphosphooctonate aldolase		
PA3636		CTP synthase	pyrG	
PA3637	9949790	conserved hypothetical protein	<u> </u>	mesJ
PA3638	0040709	acetyl-coenzyme A carboxylase carboxyl trans	accA	
PA3639	0040900	DNA polymerase III, alpha chain	dnaE	polC
PA3640	9949000	lipid A-disaccharide synthase	lpxB	lpgsB
PA3643	9949803	UDP-N-acetylglucosamine acyltransferase	IpxA	
PA3644	9949804	(3R)-hydroxymyristoyl-[acyl carrier protein] del		sefA
PA3645	0040906	UDP-3-O-[3-hydroxylauroyl] glucosamine N-ac	InxD	firA omsA
PA3646	9949600	probable outer membrane protein precursor		*
PA3647		probable outer membrane protein		
PA3648 PA3650	00/0911	1-deoxy-d-xylulose 5-phosphate reductoisome	dxr	yaeM
PA3651	0040812	phosphatidate cytidylyltransferase	cdsA	
	00/08/12	undecaprenyl pyrophosphate synthetase	uppS	yaeS
PA3652	0040944	ribosome recycling factor	frr	rrf
PA3653		uridylate kinase	pyrH	smbA
PA3654		elongation factor Ts	Itsf	
PA3655	0040047	30S ribosomal protein S2	rpsB	
PA3656		methionine aminopeptidase	map	
PA3657		hypothetical protein	1	
PA3662	9949824	conserved hypothetical protein	 	yffB
PA3664	9949826	tetrahydrodipicolinate succinylase	dapD	
PA3666	9949828	pre-hable permanes of APC transporter	1225	
PA3671	9949833	probable permease of ABC transporter	 	
PA3674	9949837	hypothetical protein		
PA3678	9949841	probable transcriptional regulator	<u> </u>	

				The state of the s
PA3681	9949844	hypothetical protein		
PA3684		hypothetical protein		
PA3685	9949849	conserved hypothetical protein	<u> </u>	
PA3688	9949852	hypothetical protein		
PA3693	9949858	conserved hypothetical protein	! 	
PA3701		peptide chain release factor 2	prfB	
PA3704	9949868	probable chemotaxis sensor/effector fusion pr	p	
PA3719	9949885	hypothetical protein	; {	
PA3715	9949891	single-stranded-DNA-specific exonuclease Re	recJ	
PA3725 PA3726	9949892	conserved hypothetical protein		yaeQ
	00/0807	hypothetical protein		
PA3730	9949091	conserved hypothetical protein		yjfJ
PA3731	0049900	hypothetical protein		
PA3733	9949900	50S ribosomal protein L19	rplS	
PA3742	9949910	tRNA (guanine-N1)-methyltransferase	trmD	
PA3743	9949911	16S rRNA processing protein	rimM	
PA3744	9949912	30S ribosomal protein S16	rpsP	
PA3745	9949913	signal recognition particle protein Ffh	ffh	
PA3746	9949914	hypothetical protein		
PA3752	9949921	Inypotnetical protein		yeaB
PA3754	9949923	hypothetical protein	 	vafK
PA3756	9949925	hypothetical protein	 	
PA3759	9949928	probable aminotransferase	 	
PA3765	9949935	hypothetical protein	 	yfhC
PA3767	9949937	conserved hypothetical protein	guaA	7
PA3769	9949940	GMP synthase	guart	
PA3773	9949944	hypothetical protein	 	
PA3776	9949947	probable transcriptional regulator	xseA	
PA3777	9949948	exodeoxyribonuclease VII large subunit	12001	
PA3782	9949954	probable transcriptional regulator	- 	
PA3784	9949956	hypothetical protein		
PA3785	9949957	conserved hypothetical protein	- [
PA3787	9949959	conserved hypothetical protein	 	
PA3788	9949960	hypothetical protein		
PA3796	9949969	hypothetical protein		
PA3800	9949973	conserved hypothetical protein	-{	gcpE
PA3803	9949976	conserved hypothetical protein	pilF	- Jaope
PA3805	994997	type 4 fimbrial biogenesis protein PilF	1 Pill	yfgB
PA3806	994997	conserved hypothetical protein	ndk	
PA3807	994998	nucleoside diphosphate kinase	HUK	yfhJ
PA3808	994998	2 conserved hypothetical protein	fdx2	lyiiio
PA3809	994998	3 ferredoxin [2Fe-2S]		
PA3810		4 heat shock protein HscA	hscA	
PA3811	994998	5 heat shock protein HscB	hscB	
PA3812	994998	6 probable iron-binding protein IscA	iscA	
PA3813	994998	7 probable iron-binding protein IscU	iscU	
PA3815	994998	9 conserved hypothetical protein	15	
PA3821	994999	5 secretion protein SecD	secD	luciC
PA3822	994999	6 conserved hypothetical protein		yajC
PA3827	995000	2 conserved hypothetical protein	<u> </u>	yjgQ
PA3828	995000	3 conserved hypothetical protein		yjgP
PA3829	995000	4 hypothetical protein	<u></u>	
PA3833	995000	8 hypothetical protein		

DA2024	9950009:valyl-tRNA synthetase	valS	
PA3834	9950010 hypothetical protein		
PA3835	9950016 conserved hypothetical protein		lybiN
PA3840			1
PA3843	9950019 hypothetical protein		
PA3850	9950027 hypothetical protein		
PA3851	9950028 hypothetical protein		
PA3854	9950031 hypothetical protein		
PA3856	9950033 hypothetical protein		
PA3857	9950034 conserved hypothetical protein		
PA3859	9950037 probable carboxylesterase		
PA3867	9950046 probable DNA invertase	······································	
PA3868	9950047 hypothetical protein		
PA3869	9950048 hypothetical protein		
PA3876	990000 Milito Oxeración Protein 2	narK2	
PA3884	9950064 hypothetical protein		
PA3886	9950066 hypothetical protein		
PA3888	9950069 probable permease of ABC transporter		
PA3890	9950071 probable permease of ABC transporter		
PA3891	9950072 probable ATP-binding component of ABC tran	5	
PA3892	9950073 conserved hypothetical protein		
PA3904	9950087 hypothetical protein		
PA3905	9950088 hypothetical protein		
PA3906	9950089 hypothetical protein		
PA3911	9950094 conserved hypothetical protein		yhbT
PA3916	9950100 molybdopterin converting factor, large subunit	moaE	
PA3917	9950101 molybdopterin converting factor, small subunit	moaD	
PA3918	9950102 molybdopterin biosynthetic protein C	moaC	
PA3936	9950122 probable permease of ABC taurine transporter		tauC
PA3940	9950127 probable DNA binding protein		
PA3960	9950149 hypothetical protein	<u> </u>	
PA3962	9950151 hypothetical protein		
PA3965	9950154 probable transcriptional regulator	<u> </u>	
PA3967	9950156 hypothetical protein	1 '	
PA3969	9950158 conserved hypothetical protein	į	
PA3973	9950163 probable transcriptional regulator		
PA3977	9950167 glutamate-1-semialdehyde 2,1-aminomutase	hemL	
PA3979	9950170 hypothetical protein	<u>{</u>	
PA3981	9950172 conserved hypothetical protein		ybeZ
PA3982	9950173 conserved hypothetical protein	!	
PA3984	9950175 apolipoprotein N-acyltransferase	Int	cutE
PA3986	9950177 hypothetical protein	<u> </u>	
PA3987	9950178 leucyl-tRNA synthetase	leuS	
PA3988	9950179 hypothetical protein	1	
PA3989	9950180 DNA polymerase III, delta subunit	holA	
PA3990	9950182 conserved hypothetical protein	1	
PA3993	9950185 probable transposase	i	
PA3996	9950188 lipoate synthase	ilipA	lip
PA3998	9950190 conserved hypothetical protein		ybeD
PA4002	9950194 rod shape-determining protein	rodA	mrdB
PA4005	9950197 conserved hypothetical protein	:	ybeB
PA4006	9950198 hypothetical protein		ybeN
	9950201 probable hydrolase	:	
PA4008	aaaozo i Ibronanie nyorolase	1	

PA4012	9950205 hypothetical protein		
PA4018.	9950211 hypothetical protein	*	and an experimental property and the second
PA4019	9950212 probable aromatic acid decarboxylase		
PA4028	9950222 hypothetical protein		
PA4029	9950224 conserved hypothetical protein	<u>!</u>	dedA
PA4031	9950226 inorganic pyrophosphatase	ippa	lipyR
PA4033	9950228 hypothetical protein	1	!
PA4037	9950232 probable ATP-binding component of ABC to	ans	
PA4043	9950239 geranyltranstransferase	ispA	j
PA4044	9950240 1-deoxyxylulose-5-phosphate synthase	dxs	
PA4047	9950243 GTP cyclohydrolase II	ribA	
PA4047	9950245 hypothetical protein		
PA4049	9950246 phosphatidylglycerophosphatase A	рдрА	
PA4050	9950247 thiamine monophosphate kinase	thiL	
	9950248 NusB protein	nusB	ssyB
PA4052	9950249 6,7-dimethyl-8-ribityllumazine synthase	ribE	ribH
PA4053	9950252 riboflavin synthase alpha chain	ribC	ribB
PA4055	9950253 riboflavin-specific deaminase/reductase	ribD	ribG
PA4056	9950254 conserved hypothetical protein	i i	ybaD
PA4057	9950256 hypothetical protein		-
PA4059	9950257 hypothetical protein		
PA4060	9950260 hypothetical protein		
PA4063	9950261 probable ATP-binding component of ABC t	rans	
PA4064	9950266 probable epimerase		
PA4068	9950274 hypothetical protein		
PA4076	9950275 probable transcriptional regulator		
PA4077	9950282 probable pili assembly chaperone		
PA4083	9950298 probable alcohol dehydrogenase (Zn-depe	nde	ydjL
PA4097	9950300 hypothetical protein		
PA4099 PA4104	9950305 conserved hypothetical protein		
PA4104 PA4107	9950309 hypothetical protein		
	9950317 spermidine acetyltransferase		bltD
PA4114 PA4121	9950324 conserved hypothetical protein		
PA4121	9950325 conserved hypothetical protein		
PA4122	9950329 5-carboxymethyl-2-hydroxymuconate isom	erashpcD	
PA4125	9950339 hypothetical protein		
PA4134	9950346 hypothetical protein		
PA4141	9950355 conserved hypothetical protein		acoX
PA4149	9950357 acetoin catabolism protein AcoB	acoB	
	9950364 probable transcriptional regulator	T I	
PA4157	9950372 hypothetical protein		
PA4164	9950375 probable oxidoreductase		yafB
PA4167	9950377 conserved hypothetical protein		
PA4169	9950378 hypothetical protein		
PA4170	9950379 probable protease		
PA4171	9950379 probable protease 9950383 probable transcriptional regulator		
PA4174	9950385 peptidyl-prolyl cis-trans isomerase C2	ppiC2	
PA4176	9950390 hypothetical protein	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	
PA4181	9950391 hypothetical protein		
PA4182	9950392 hypothetical protein		
PA4183	9950400 probable FAD-dependent monooxygenase		
PA4190			
PA4209	9950421 probable O-methyltransferase		

PA4210 .	9950423 probable phenazine biosynthesis protein		phzA1
PA4210	9950424 probable phenazine biosynthesis protein		phzB1
	9950425 phenazine biosynthesis protein PhzC		phzC1
PA4212	9950428 probable phenazine biosynthesis protein		phzF1
PA4215	9950430 probable pyridoxamine 5'-phosphate oxidase		phzG1
PA4216	9950433 bynothotical protein		yfpB
PA4219	9950433 hypothetical protein 9950446 salicylate biosynthesis protein PchB	pchB	1 .
PA4230	9950446 sailcylate biosynthesis protein Forib	ssb	
PA4232	9950448 single-stranded DNA-binding protein	rplQ	
PA4237	9950454 50S ribosomal protein L17	rpoA	
PA4238	9950455 DNA-directed RNA polymerase alpha chain	rpsD	
PA4239	9950456 30S ribosomal protein S4	rpsK	
PA4240	9950457 30S ribosomal protein S11	rpsM	
PA4241 i	9950458 30S ribosomal protein S13		
PA4242	9950459 50S ribosomal protein L36	rpmJ	prlA
PA4243	9950460 secretion protein SecY	secY	IPIA
PA4244	9950461 50S ribosomal protein L15	rplO	
PA4245	9950462 50S ribosomal protein L30	rpmD	
PA4246	9950463 30S ribosomal protein S5	rpsE	
PA4247	9950464 50S ribosomal protein L18	rplR	
PA4248	9950465 50S ribosomal protein L6	rplF	
PA4249	9950466 30S ribosomal protein S8	rpsH	
PA4250	9950467 30S ribosomal protein S14	rpsN	
PA4251	9950468 50S ribosomal protein L5	rpIE	
PA4252	9950469 50S ribosomal protein L24	гріХ	
PA4253	9950470 50S ribosomal protein L14	rpIN	
PA4254	9950471 30S ribosomal protein S17	rpsQ	
PA4255	9950472 50S ribosomal protein L29	rpmC	
PA4256	9950473 50S ribosomal protein L16	rpIP	
PA4257	9950474 30S ribosomal protein S3	rpsC	
PA4258	9950475 50S ribosomal protein L22	rpiV	
PA4259	9950476 30S ribosomal protein S19	rpsS	
PA4260	9950477 50S ribosomal protein L2	rpiB	
PA4261	9950478 50S ribosomal protein L23	rplW	
PA4262	9950479 50S ribosomal protein L4	rplD	
PA4263	9950480 50S ribosomal protein L3	rplC	
PA4264	9950482 30S ribosomal protein S10	rpsJ	
PA4267	9950485 30S ribosomal protein S7	rpsG	·
PA4268	9950486 30S ribosomal protein S12	IrpsL	str
PA4269	9950487 DNA-directed RNA polymerase beta* chain	rpoC	
PA4270	9950488 DNA-directed RNA polymerase beta chain	rpoB	
PA4271	9950490 50S ribosomal protein L7 / L12	rplL	
PA4272	9950491 50S ribosomal protein L10	rplJ	
PA4273	9950492 50S ribosomal protein L1	rplA	
PA4274	9950493 50S ribosomal protein L11	rplK	
PA4275	9950494 transcription antitermination protein NusG	nusG	
PA4276	9950495 secretion protein SecE	secE	prlG
PA4279	9950498 hypothetical protein	<u> </u>	
PA4295	9950516 hypothetical protein	<u> </u>	
PA4296	9950518 probable two-component response regulator	<u> </u>	
PA4298	9950520 hypothetical protein	-,-	
PA4299	9950521 hypothetical protein	!	
PA4305	9950527 hypothetical protein		1

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PA4450	9950685 UDP-N-acetylglucosamine 1-carboxyvinyltran	<u>émurA</u>		
PA4452	9950687 conserved hypothetical protein		n. Distribution of the last of the second state of the second state of the last of the second state of the second	 .
PA4453	9950688 conserved hypothetical protein	<u>:</u>		
PA4454	9950689 conserved hypothetical protein		yrbD	
PA4455	9950690 probable permease of ABC transporter		lyrbE	
PA4457	9950693 conserved hypothetical protein		yrbH kpsF	
PA4459	9950695 conserved hypothetical protein	į	yrbK	
PA4460	9950696 conserved hypothetical protein	1	yhbN	
PA4461 :	9950697 probable ATP-binding component of ABC train	าร	yhbG	
	9950698 RNA polymerase sigma-54 factor	rpoN	ntrA	
PA4462	9950699 conserved hypothetical protein	1	lyhbH	
PA4463	9950700 nitrogen regulatory IIA protein	ptsN		
PA4464	9950700 probable phosphoryl carrier protein	1		
PA4466	9950707 hypothetical protein	 	faigA	
PA4471	9950707 hypothetical protein 9950718 rod shape-determining protein MreC	ImreC		
PA4480	9950719 rod shape-determining protein MreB	mreB	envB rodY	<i></i>
PA4481	9950719 rod snape-determining protein wies	gatC		
PA4482	9950720 Glu-tRNA(Gln) amidotransferase subunit C	gatA		
PA4483	9950721 Glu-tRNA(Gln) amidotransferase subunit A	gatB		
PA4484	9950722 Glu-tRNA(Gln) amidotransferase subunit B	gaib		
PA4485	9950723 conserved hypothetical protein			
PA4492	9950730 conserved hypothetical protein			
PA4499	9950738 probable transcriptional regulator			
PA4507	9950747 hypothetical protein	nadC		
PA4524	9950766 nicotinate-nucleotide pyrophosphorylase	pilA		
PA4525	9950767 type 4 fimbrial precursor PilA			
PA4526	9950768 type 4 fimbrial biogenesis protein PilB	pilB		
PA4527	9950770 still frameshift type 4 fimbrial biogenesis prot	erpiic		
PA4529	9950772 conserved hypothetical protein			
PA4530	9950773 conserved hypothetical protein			
PA4537	9950780 hypothetical protein		(.e)	
PA4544	9950788 pseudouridine synthase	rluD	yfil	
PA4547	9950791 two-component response regulator PilR	pilR		
PA4552	9950797 type 4 fimbrial biogenesis protein PilW	pilW		
PA4553	9950798 type 4 fimbrial biogenesis protein PilX	pilX		
PA4557	9950802 LytB protein	lytB		
PA4559	9950804 prolipoprotein signal peptidase	IspA		
PA4560	9950805 isoleucyl-tRNA synthetase	ileS		
PA4561	9950806 riboflavin kinase/FAD synthase	ribF		
PA4563	9950809 30S ribosomal protein S20	rpsT		
PA4564	9950810 conserved hypothetical protein		creA	
PA4565	9950811 glutamate 5-kinase	proB		
PA4566	9950812 GTP-binding protein Obg	obg		
PA4567	9950813 50S ribosomal protein L27	,rpmA		
PA4568	9950814 50S ribosomal protein L21	[rplU		
PA4569	9950815 octaprenyl-diphosphate synthase	ispB	cel	
PA4574	9950821 conserved hypothetical protein	ļ	yqhA	
PA4575	9950822 hypothetical protein			
PA4577	9950824 hypothetical protein			
PA4577	9950834 hypothetical protein			
	9950850 transcriptional regulator NfxB	nfxB		
PA4600	9950853 hypothetical protein			
PA4603	9950861 hypothetical protein	<u> </u>		

				and the second s
PA4611	9950862	nypothetical protein		
PA4617	9950868	conserved hypothetical protein		jygjO
PA4630	9950883	hypothetical protein		
PA4636	9950890	hypothetical protein		
PA4637	9950891	hypothetical protein		
PA4638	9950892	hypothetical protein		***************************************
PA4642		hypothetical protein		
PA4644	9950897	hypothetical protein		
PA4646	9950899	uracil phosphoribosyltransferase	ирр	
PA4649	9950903	hypothetical protein		
PA4651	9950905	probable pill assembly chaperone		
PA4655	9950909	ferrochelatase	hemH	visA
PA4662		glutamate racemase	murl	
PA4663	9950918	molybdopterin biosynthesis MoeB protein	moeB	chIN
PA4665	9950920	peptide chain release factor 1	prfA	rf1
PA4666	9950921	glutamyl-tRNA reductase	hemA	hem1; glutR
PA4668	9950923	probable lipoprotein localization protein LolB		lolB
PA4669	9950924	isopentenyl monophosphate kinase	ipk	ychB !
PA4670	9950924	ribose-phosphate pyrophosphokinase	prs	prsA
PA4671	9950927	probable ribosomal protein L25		rplY
PA4672		peptidyl-tRNA hydrolase		pth
PA4674	9950920	conserved hypothetical protein		vapl
	9950930	probable carbonic anhydrase		yadF
PA4676	9930932	hypothetical protein		
PA4679	9950933	hypothetical protein		
PA4681	0050050	phosphatidylserine synthase	pssA	
PA4693	9950950	acetolactate synthase large subunit	lilvl	
PA4696 PA4697	9950955	hypothetical protein		-
PA4698		hypothetical protein		yqcC
PA4699		hypothetical protein		
PA4702		hypothetical protein		
PA4706	9950964	probable ATP-binding component of ABC tran	is	phuV
PA4700 PA4711		hypothetical protein		
PA4711	9950977	hypothetical protein		
PA4718	9950988	2-amino-4-hydroxy-6-hydroxymethyldihydropte	folK	
PA4729	9950989	3-methyl-2-oxobutanoate hydroxymethyltransf	panB	
PA4731	9950993	aspartate 1-decarboxylase precursor	panD	
PA4731	0050002	glucose-6-phosphate isomerase	pgi	
PA4737	9950998	hypothetical protein	1	
PA4738	9950990	conserved hypothetical protein		yjbJ
PA4739	9950995	conserved hypothetical protein		
PA4740	9951000	polyribonucleotide nucleotidyltransferase	pnp	
	9951002	3 30S ribosomal protein S15	rpsO	
PA4741	9951000	translation initiation factor IF-2	infB	
PA4744	005100	7 N utilization substance protein A	nusA	
PA4745	005100	B conserved hypothetical protein	1	yhbC
PA4746		9 secretion protein SecG	secG	
PA4747		O triosephosphate isomerase	tpiA	tpi
PA4748		1 phosphoglucosamine mutase	glmM	yhbF, mrsA
PA4749		2 dihydropteroate synthase	folP	dhpS
PA4750	995101	5 cell division protein FtsJ	ftsJ	
PA4752	995101	6 conserved hypothetical protein	1	yhbY
PA4753	1 990 1011	ofcouseried Hypotherical brotein		

			veaS
PA4757	9951020 conserved hypothetical protein	<u> </u>	yeas
PA4759	9951022 dihydrodipicolinate reductase	∖dapB	The state of the s
PA4762	9951026 heat shock protein GrpE	grpE	
PA4764	9951028 ferric uptake regulation protein	fur	
PA4765	9951029 outer membrane lipoprotein OmlA	!omlA	oprX
PA4767	9951031 conserved hypothetical protein		yfjG
PA4773	9951038 hypothetical protein		
PA4776	9951041 probable two-component response regulato	r i	
PA4778	9951043 probable transcriptional regulator		ybbl
PA4782	9951047 hypothetical protein		
PA4788	9951054 hypothetical protein		
PA4789	9951055 conserved hypothetical protein		
PA4790	9951056 conserved hypothetical protein		smtA
PA4792	9951058 conserved hypothetical protein		
PA4797	9951064 probable transposase		
PA4802	9951069 hypothetical protein		
PA4809	9951077 FdhE protein	fdhE	•
PA4813	9951080 lipase LipC	[lipC	
PA4823	9951091 hypothetical protein		
PA4826	9951095 hypothetical protein		
PA4828	9951097 conserved hypothetical protein		
PA4831	9951100 probable transcriptional regulator		
PA4841	9951111 conserved hypothetical protein		
PA4847	9951118 biotin carboxyl carrier protein (BCCP)	accB	fabE
PA4848	9951119 biotin carboxylase	accC	
PA4850	9951121 ribosomal protein L11 methyltransferase	prmA	
PA4853	9951124 DNA-binding protein Fis	fis	
PA4861	9951133 probable ATP-binding component of ABC tr	ans	
PA4864	9951137 urease accessory protein	lureD	
PA4866	9951139 conserved hypothetical protein	i	
PA4868	9951141 urease alpha subunit	ureC	
PA4870	9951143 conserved hypothetical protein	j	ybil
PA4871	9951144 hypothetical protein	1	
PA4874	9951148 conserved hypothetical protein		psiF
PA4875	9951149 hypothetical protein		
PA4878	9951152 probable transcriptional regulator		
PA4885	9951159 two-component response regulator	irlR	
PA4887	9951161 probable MFS transporter		
PA4890	9951165 conserved hypothetical protein		yijC
PA4892	9951167 urease accessory protein UreF	ureF	
PA4894	9951169 hypothetical protein		
PA4895	9951170 probable transmembrane sensor		
PA4906	9951182 probable transcriptional regulator		
PA4908	9951185 hypothetical protein		
PA4906	9951193 hypothetical protein		
PA4916 PA4920	9951198 NH3-dependent NAD synthetase	nadE	
PA4920	9951201 conserved hypothetical protein		
	9951203 conserved hypothetical protein		
PA4925	9951204 conserved hypothetical protein		
PA4926	9951210 replicative DNA helicase	dnaB	
PA4931	9951213 30S ribosomal protein S18	rpsR	
PA4934	9951214 30S ribosomal protein S6	rpsF	
PA4935	33312141303 Hb0S0Hai protein 30	<u>i.F.z.</u>	

		ipurA	
PA4938	9951218 adenylosuccinate synthetase	ibaiv	yjeT
PA4940	9951220 conserved hypothetical protein	<u> </u>	
PA4944	9951224 conserved hypothetical protein	1	hfq
PA4945	9951225 delta 2-isopentenylpyrophosphate transfera	ise imiaA	1.1.2
PA4948	9951228 conserved hypothetical protein		yjeE
PA4952	9951233 conserved hypothetical protein		lyjeQ
PA4956	9951237 thiosulfate sulfurtransferase	rhdA	
PA4961	9951243 hypothetical protein		
PA4962	9951244 conserved hypothetical protein		ybcl
PA4964	9951246 topoisomerase IV subunit A	parC	
PA4965	9951247 hypothetical protein		
PA4966	9951248 hypothetical protein		
PA4967	9951249 topoisomerase IV subunit B	parE	
PA4969	9951252 conserved hypothetical protein		icc
PA4972	9951255 hypothetical protein	}	
PA4980	9951263 probable enovl-CoA hydratase/isomerase		
PA4988	9951272 3-deoxy-D-manno-octulosonic-acid (KDO)	tranwaaA	kdtA
PA4990	9951275 SMR multidrug efflux transporter		
PA4991	9951276 hypothetical protein		
PA4992	9951277 hypothetical protein		
PA4997	9951282 transport protein MsbA	msbA	
PA4998	9951283 conserved hypothetical protein		
PA5006	9951292 hypothetical protein		
PA5007	9951293 hypothetical protein		wapQ inaA
PA5008	9951294 hypothetical protein		wapP waaX
PA5009	9951295 lipopolysaccharide core biosynthesis prote	in WwaaP	rfaP
PA5010	9951296 UDP-glucose:(heptosyl) LPS alpha 1,3-glu	coswaaG	rfaG
PA5010	9951297 heptosyltransferase I	waaC	rfaC
PA5012	9951298 heptosyltransferase II	waaF	rfaF
PA5012	9951317 conserved hypothetical protein		
PA5032	9951321 probable transcriptional regulator		
PA5032	9951322 hypothetical protein		-
PA5034	9951323 uroporphyrinogen decarboxylase	hemE	
PA5034	9951329 shikimate kinase	aroK	
PA5044	9951334 type 4 fimbrial biogenesis protein PilM	Mliq	
PA5044	9951341 primosomal protein N'	priA	
PA5050	9951342 arginyl-tRNA synthetase	argS	
PA5051	9951343 hypothetical protein		
PA5052	9951353 conserved hypothetical protein		phal
PA5063	9951355 ubiquinone biosynthesis methyltransferas	e UblubiE	
	9951356 hypothetical protein		
PA5064	9951357 conserved hypothetical protein		aarF yigR
PA5065	9951360 phosphoribosyl-ATP pyrophosphohydrola	se hisE	
PA5067	9951361 translocation protein TatA	tatA.	mttA yigT
PA5068	9951364 conserved hypothetical protein		:
PA5071	9951365 probable chemotaxis transducer		
PA5072			
PA5081	9951375 hypothetical protein		
PA5085	9951379 probable transcriptional regulator	fbp	cbbF, cfxF
PA5110	9951406 fructose-1,6-bisphosphatase	gloA3	glo1
PA5111	9951408 lactoylglutathione lyase	Igiona	
PA5116	9951413 probable transcriptional regulator	Idla ^	
PA5119	9951417 glutamine synthetase	[glnA	

	005142716	secretion protein SecB	secB	
PA5128	995142718	eluteredevin	grx	
PA5129	995142019	glutaredoxin conserved hypothetical protein	1	yibN
PA5130 .	995142910	conserved hypothetical protein	pgm	!vibO
PA5131	9951430	phosphoglycerate mutase	 Pg	
PA5132	99514311	nypothetical protein	ihisH1	1
PA5142	9951442	glutamine amidotransferase	11115111	
PA5144	9951444	nypothetical protein	-	i luan V
PA5148	9951448	conserved hypothetical protein	:	yggX
PA5154	9951455	probable permease of ABC transporter	 	1-6-0
PA5161	9951463	dTDP-D-glucose 4,6-dehydratase	rmlB	rfbB
PA5162	9951464	dTDP-4-dehydrorhamnose reductase	rmID	rfbD
PA5163	9951465	glucose-1-phosphate thymidylyltransferase	rmlA	rfbA
PA5164	9951466	dTDP-4-dehydrorhamnose 3,5-epimerase	rmlC	rfbC
PA5173	9951476	carbamate kinase	larcC	
PA5176	9951479	conserved hypothetical protein		yrfE
PA5178	9951481	conserved hypothetical protein		
PA5182	9951486	hypothetical protein		
PA5187	9951491	probable acyl-CoA dehydrogenase		
PA5190	9951495	probable nitroreductase		
PA5190	9951500	probable heat shock protein		yrfH
	0051520	probable FAD-dependent monooxygenase		visC
PA5221	0051529	hypothetical protein		
PA5222	9951530	aminopeptidase P	рерР	
PA5224	990 1002	hypothetical protein	<u> </u>	
PA5225	9951533	conserved hypothetical protein		ygfE
PA5227	9951535	conserved hypothetical protein		
PA5229	9951537	conserved hypothetical protein		yigC
PA5237	9951546	transcription termination factor Rho	rho	
PA5239	9951548	transcription termination ractor ratio	trxA	
PA5240	9951549	thioredoxin	1475	yigl
PA5246	9951556	conserved hypothetical protein		yail
PA5247	9951557	conserved hypothetical protein	hemD	- Jun
PA5259	9951570	uroporphyrinogen-III synthetase	hemC	рорЕ
PA5260	9951571	porphobilinogen deaminase	Tieillo	cyaY
PA5275	9951588	conserved hypothetical protein	lppL	Cyai
PA5276	9951589	lipopeptide LppL precursor	dapF	
PA5278		diaminopimelate epimerase	<u>uapr</u>	- Juia B
PA5281	9951594	probable hydrolase		yigB
PA5288	9951602	nitrogen regulatory protein P-II 2	glnK	
PA5296	9951611	ATP-dependent DNA helicase Rep	rep	
PA5300	9951616	cytochrome c5	сусВ	
PA5303	9951619	conserved hypothetical protein		
PA5316	9951633	50S ribosomal protein L28	rpmB	
PA5319	9951636	DNA repair protein RadC	radC	
PA5320	9951637	DNA/pantothenate metabolism flavoprotein	dfp	
PA5321	9951638	deoxyuridine 5'-triphosphate nucleotidohydro	oladut	
PA5325	9951643	hypothetical protein		
PA5328	9951646	probable cytochrome c(mono-heme type)		
PA5330	995164	8 hypothetical protein		
	005164	9 orotate phosphoribosyltransferase	ругЕ	
PA5331	005165	2 conserved hypothetical protein		
PA5333	990 100	3 ribonuclease PH	rph	
PA5334		4 conserved hypothetical protein		yicC

PA5336	9951655 guanylate kinase	gmk	
PA5339	9951658 conserved hypothetical protein		
PA5347	9951667 hypothetical protein		
PA5350	9951670 rubredoxin		
PA5351	9951671 rubredoxin		
PA5358	9951678 4-hydroxybenzoate-octaprenyl transferase	ubiA	
PA5364	9951685 probable two-component response regulator		
PA5381	9951704 hypothetical protein		1
PA5385	9951709 hypothetical protein		1
PA5390	9951714 probable peptidic bond hydrolase		ì
PA5396	9951721 hypothetical protein		
PA5403	9951729 probable transcriptional regulator	ļ	
PA5404	9951730 hypothetical protein	ĺ	
PA5406	9951732 hypothetical protein		
PA5408	9951734 hypothetical protein		
PA5417	9951744 sarcosine oxidase delta subunit	soxD	
PA5457	9951788 hypothetical protein		
PA5460	9951792 hypothetical protein		
PA5465	9951797 hypothetical protein		:
PA5469	9951801 conserved hypothetical protein		
PA5470	9951802 probable peptide chain release factor		prfH
PA5480	9951813 hypothetical protein		
PA5482	9951816 hypothetical protein		•
PA5496	9951831 hypothetical protein		
PA5503	9951839 probable ATP-binding component of ABC trans	ş	
PA5526	9951864 hypothetical protein		
PA5529	9951867 probable sodium/proton antiporter		
PA5531	9951869 TonB protein	tonB	
PA5533	9951871 hypothetical protein		
PA5534	9951873 hypothetical protein		
PA5543	9951882 hypothetical protein		
PA5549	9951889 glucosaminefructose-6-phosphate aminotral	nˈglmS	
PA5552	9951892 glucosamine-1-phosphate acetyltransferase/N	lfglmU	gcaD
PA5553	9951893 ATP synthase epsilon chain	atpC	uncC papG
PA5554	9951894 ATP synthase beta chain	atpD	uncD papB
PA5555	9951895 ATP synthase gamma chain	atpG	uncG papC
PA5556	9951896 ATP synthase alpha chain	atpA	uncA papA
PA5557	9951897 ATP synthase delta chain	atpH	uncH papE
PA5558	9951898 ATP synthase B chain	atpF	uncF papF
PA5559	9951899 atp synthase C chain	atpE	uncE papH
PA5560	9951900 ATP synthase A chain	atpB	uncB papD
PA5561	9951901 ATP synthase protein I	atpl	uncl
PA5562	9951903 chromosome partitioning protein Spo0J	spoOJ	
PA5566	9951907 hypothetical protein		
PA5568	9951909 conserved hypothetical protein		yidC
PA5569	9951910 ribonuclease P protein component	rnpA	
PA5570	9951911 50S ribosomal protein L34	rpmH	

Part of Palmany Edination	Rancession	Rancearo
DNA replication, recombination, modificat	483	2027
DNA replication, recombination, modificat	4275	
Hypothetical, unclassified, unknown	8339	
Translation, post-translational modification		10434
Translation, post-translational modification	13435	12488
Cell wall / LPS / capsule	14235	15122
Hypothetical, unclassified, unknown	17217	16900
Hypothetical, unclassified, unknown	24001	24558
Hypothetical, unclassified, unknown	27646	28632
Hypothetical, unclassified, unknown	36270	35905
Amino acid biosynthesis and metabolism	37893	37087
Hypothetical, unclassified, unknown	40190	40405
Hypothetical, unclassified, unknown	40589	40816
Hypothetical, unclassified, unknown	56546	56941
Hypothetical, unclassified, unknown	61879	62388
Hypothetical, unclassified, unknown	68616	68188
Hypothetical, unclassified, unknown	69272	69526
Hypothetical, unclassified, unknown	70091	69543
Hypothetical, unclassified, unknown	70636	70130
Hypothetical, unclassified, unknown	72680	73384
Adaptation, protection	73468	73923
Hypothetical, unclassified, unknown	74034	74267
Hypothetical, unclassified, unknown	74716	74279
Hypothetical, unclassified, unknown	78097	77432
Hypothetical, unclassified, unknown	80752	81027
Hypothetical, unclassified, unknown	81116	82174
Hypothetical, unclassified, unknown	83318	82404
Hypothetical, unclassified, unknown	98218	97754
Hypothetical, unclassified, unknown	100124	101158
Hypothetical, unclassified, unknown	115045	114611
Hypothetical, unclassified, unknown	119127	120164
Hypothetical, unclassified, unknown	121346	122266
Energy metabolism	127378	128502
Hypothetical, unclassified, unknown	131792	131583
Hypothetical, unclassified, unknown	132577	133155
Energy metabolism	134319	
Hypothetical, unclassified, unknown	135259	135894
Hypothetical, unclassified, unknown	136386	
Hypothetical, unclassified, unknown	136518	136991
Transport of small molecules	138818	
Transcriptional regulators	140216	
Hypothetical, unclassified, unknown	143848	
Hypothetical, unclassified, unknown	144072	143845
Hypothetical, unclassified, unknown	145542	145883
Hypothetical, unclassified, unknown	149425	
Transcriptional regulators	150906	151823
Hypothetical, unclassified, unknown	153696	
Adaptation, protection	158199	
Nucleotide biosynthesis and metabolism	163426	
Hypothetical, unclassified, unknown	165737	
Transcriptional regulators	169361	169906

Carbon compound catabolism	175503	176108
Transcriptional regulators	182768	183706
Hypothetical, unclassified, unknown	184287	184439
Transcriptional regulators	191697	192362
Hypothetical, unclassified, unknown	194179	193799
Hypothetical, unclassified, unknown	194748	194206
Putative enzymes	207071	207823
Carbon compound catabolism	209533	207923
Transport of small molecules	210460	209621
Hypothetical, unclassified, unknown	213819	214634
Hypothetical, unclassified, unknown	214631	215512
Hypothetical, unclassified, unknown	229738	229526
Putative enzymes	232000	230543
Transport of small molecules	233100	232066
Transport of small molecules	233932	233123
Transport of small molecules	234849	233929
Transcriptional regulators	236218	237111
Hypothetical, unclassified, unknown	238896	239777
Carbon compound catabolism	240071	240934
Hypothetical, unclassified, unknown	241753	242445
Transport of small molecules	243841	244605
Transcriptional regulators	262557	263498
Transcriptional regulators	266616	267395
Hypothetical, unclassified, unknown	268704	269519
Transcriptional regulators	275772	276440
Hypothetical, unclassified, unknown	277334	276480
Amino acid biosynthesis and metabolism	277777	277331
Hypothetical, unclassified, unknown	282757	282323
Hypothetical, unclassified, unknown	283553	282912
Hypothetical, unclassified, unknown	289390	289205
Hypothetical, unclassified, unknown	. 293304	291154
Hypothetical, unclassified, unknown	293798	293301
Hypothetical, unclassified, unknown	299497	299081
Transport of small molecules	309092	307878
Transcriptional regulators	313227	313925
Transport of small molecules	314927	313938
Hypothetical, unclassified, unknown	318148	317966
Hypothetical, unclassified, unknown	350841	350089
Hypothetical, unclassified, unknown	352164	351610
Hypothetical, unclassified, unknown	359982	360332
Energy metabolism	371833	371162
Hypothetical, unclassified, unknown	373725	374192
Hypothetical, unclassified, unknown	378096	378575
Hypothetical, unclassified, unknown	382792	382037
Fatty acid and phospholipid metabolism	383727	384527
Nucleotide biosynthesis and metabolism	384733	385527
Biosynthesis of cofactors, prosthetic grou		393814
Hypothetical, unclassified, unknown	402020	402598
Energy metabolism	406498	406247
Central intermediary metabolism	407098	
Hypothetical, unclassified, unknown	413654	
Hypothetical, unclassified, unknown	414529	413933
C. Abanianiani animanani animani		

Protein secretion/export apparatus	417527	418894
Transcriptional regulators	420683	421537
Hypothetical, unclassified, unknown	421602	422207
Hypothetical, unclassified, unknown	423460	423660
Hypothetical, unclassified, unknown	427120	426863
Hypothetical, unclassified, unknown	439991	440395
Nucleotide biosynthesis and metabolism	445691	444687
Transcriptional regulators	446227	445715
Hypothetical, unclassified, unknown	446773	446339
Hypothetical, unclassified, unknown	447342	446773
Biosynthesis of cofactors, prosthetic grou	449384	448431
Motility & Attachment	453239	454114
Transcriptional regulators	463079	463873
Hypothetical, unclassified, unknown	470081	<u>4</u> 70650
Transport of small molecules	476333	477790
Hypothetical, unclassified, unknown	484404	484838
Hypothetical, unclassified, unknown	496478	496362
Transport of small molecules	496871	498361
Related to phage, transposon, or plasmid	501120	500104
Hypothetical, unclassified, unknown	502599	501376
Transcriptional regulators	504121	505029
Hypothetical, unclassified, unknown	510499	509825
Adaptation, protection	514775	514984
Hypothetical, unclassified, unknown	526877	527179
Hypothetical, unclassified, unknown	535085	535489
Transcriptional regulators	535539	536108
Transcriptional regulators	539143	538217
Transcriptional regulators	540735	539785
Hypothetical, unclassified, unknown	549614	549294
Putative enzymes	550381	549656
Hypothetical, unclassified, unknown	550813	550520
Putative enzymes	552746	552994
Hypothetical, unclassified, unknown	558361	557354
Biosynthesis of cofactors, prosthetic grou	560808	562013
Biosynthesis of cofactors, prosthetic grou	562006	
Biosynthesis of cofactors, prosthetic grou		563545
Biosynthesis of cofactors, prosthetic grou	563549	564235
Hypothetical, unclassified, unknown	564344	
Biosynthesis of cofactors, prosthetic grou	576040	
Transcriptional regulators	586663	
Putative enzymes	590105	
Transcriptional regulators	594580	
Hypothetical, unclassified, unknown	598608	
Hypothetical, unclassified, unknown	600176	·
Hypothetical, unclassified, unknown	600426	
Hypothetical, unclassified, unknown	602141	
Central intermediary metabolism	604896	
Hypothetical, unclassified, unknown	609999	
Energy metabolism	611281	
Hypothetical, unclassified, unknown	612517	
Carbon compound catabolism	613338	
Hypothetical, unclassified, unknown	617549	616371

Hypothetical, unclassified, unknown	620488	620135
Hypothetical, unclassified, unknown	621695	622033
Hypothetical, unclassified, unknown	622726	622884
Hypothetical, unclassified, unknown	624199	623852
Hypothetical, unclassified, unknown	624803	624189
Hypothetical, unclassified, unknown	629884	628763
Hypothetical, unclassified, unknown	638830	638381
Translation, post-translational modification	639115	638900
Translation, post-translational modification	639316	640341
Biosynthesis of cofactors, prosthetic grou	641073	641426
Hypothetical, unclassified, unknown	643714	643208
Hypothetical, unclassified, unknown	649263	648931
Hypothetical, unclassified, unknown	650538	650158
Biosynthesis of cofactors, prosthetic grou	652483	651497
Chaperones & heat shock proteins	653772	652480
Adaptation, protection	656527	653753
Energy metabolism	669415	670089
Transcriptional regulators	673091	672777
Transcriptional regulators	673961	673191
Hypothetical, unclassified, unknown	674667	675026
Hypothetical, unclassified, unknown	675390	675839
Related to phage, transposon, or plasmid	677083	677409
Hypothetical, unclassified, unknown	685846	686718
Hypothetical, unclassified, unknown	686693	686899
Related to phage, transposon, or plasmid	688605	688967
Related to phage, transposon, or plasmid	689236	689466
Related to phage, transposon, or plasmid	690420	690674
Hypothetical, unclassified, unknown	693596	694366
Hypothetical, unclassified, unknown	698932	699720
Hypothetical, unclassified, unknown	6997.44	700835
Related to phage, transposon, or plasmid	700835	701170
Hypothetical, unclassified, unknown	701477	702529
Related to phage, transposon, or plasmid	702529	702831
Related to phage, transposon, or plasmid	702828	703058
Transcriptional regulators	706672	706028
Hypothetical, unclassified, unknown	706944	707366
Hypothetical, unclassified, unknown	709182	708535
Hypothetical, unclassified, unknown	714247	713279
Hypothetical, unclassified, unknown	714686	714264
Hypothetical, unclassified, unknown	717231	717581
Protein secretion/export apparatus	737530	737081
Hypothetical, unclassified, unknown	737677	738108
Protein secretion/export apparatus	738485	738111
Protein secretion/export apparatus	741335	741928
Protein secretion/export apparatus	744333	745742
Protein secretion/export apparatus	745742	746956
Hypothetical, unclassified, unknown	748662	749774
Hypothetical, unclassified, unknown	770156	770818
Hypothetical, unclassified, unknown	770847	771326
Hypothetical, unclassified, unknown	772275	772700
Hypothetical, unclassified, unknown	775321	774416
Putative enzymes	778181	776787
Fulauve enzymes		

Putative enzymes	779208	778309
Transcriptional regulators	782113	781259
Hypothetical, unclassified, unknown	782229	782525
Central intermediary metabolism	782570	782965
Hypothetical, unclassified, unknown	783833	783576
Hypothetical, unclassified, unknown	784698	785174
Hypothetical, unclassified, unknown	785969	786925
Hypothetical, unclassified, unknown	786928	788253
Related to phage, transposon, or plasmid	789144	789356
Related to phage, transposon, or plasmid	790166	790600
Related to phage, transposon, or plasmid	795793	796776
Hypothetical, unclassified, unknown	797251	797598
Putative enzymes	798827	797925
Transcription, RNA processing and degra		801275
Hypothetical, unclassified, unknown	802239	801967
Hypothetical, unclassified, unknown	805228	805473
Hypothetical, unclassified, unknown	809882	809574
Hypothetical, unclassified, unknown	828344	827400
Secreted Factors (toxins, enzymes, alginated)		832498
Protein secretion/export apparatus	835523	837322
Protein secretion/export apparatus	837328	838182
Protein secretion/export apparatus Translation, post-translational modification		840324
Translation, post-translational modification	844295	843723
Hypothetical, unclassified, unknown	845682	845278
Hypothetical, unclassified, unknown	858646	858951
Transport of small molecules Hypothetical, unclassified, unknown	859007	860170
Hypothetical, unclassified, unknown	866451	865636
Hypothetical, unclassified, unknown	881077	881400
Hypothetical, unclassified, unknown	883216	
Hypothetical, unclassified, unknown	885635	<u> </u>
Transcriptional regulators	893041	893994
Hypothetical, unclassified, unknown	895668	<u> </u>
Hypothetical, unclassified, unknown	896416	
Hypothetical, unclassified, unknown	898886	
Hypothetical, unclassified, unknown	900165	
Hypothetical, unclassified, unknown	901046	
Putative enzymes	903692	
Chaperones & heat shock proteins	913086	
Hypothetical, unclassified, unknown	929084	
Hypothetical, unclassified, unknown	930476	
Putative enzymes	932725	
Cell division	935989	
Hypothetical, unclassified, unknown	942648	
Hypothetical, unclassified, unknown	948776	
Hypothetical, unclassified, unknown	949280	
Hypothetical, unclassified, unknown	950648	
Cell wall / LPS / capsule		
Amino acid biosynthesis and metabolism	955722	
Hypothetical, unclassified, unknown	96254	
Putative enzymes	90254	
Hypothetical, unclassified, unknown	98424	
Hypothetical, unclassified, unknown		
Translation, post-translational modification	on 986811	0 303442

Amino acid biosynthesis and metabolism	989590	990828
Transcriptional regulators	991013	991198
Transcriptional regulators	992543	991830
Hypothetical, unclassified, unknown	993409	993783
Hypothetical, unclassified, unknown	993776	994051
Transport of small molecules	996038	997486
Hypothetical, unclassified, unknown	1007548	1007234
Carbon compound catabolism	1012972	1011983
Amino acid biosynthesis and metabolism	1020708	1021607
Hypothetical, unclassified, unknown	1027445	1027984
Hypothetical, unclassified, unknown	1030151	1029825
Nucleotide biosynthesis and metabolism	1032763	1032095
Nucleotide biosynthesis and metabolism	1033824	1032763
Hypothetical, unclassified, unknown	1035277	1035981
Putative enzymes	1039968	1040432
Putative enzymes	1040432	1040707
Translation, post-translational modification		1041689
Hypothetical, unclassified, unknown	1046462	1046671
Adaptation, protection	1048019	1047549
Transport of small molecules	1053848	1054543
Transport of small molecules	1054566	1055006
Transport of small molecules	1055009	1056052
Transport of small molecules	1056049	1057347
Transport of small molecules	1057400	1057906
Hypothetical, unclassified, unknown	1059622	1060296
Hypothetical, unclassified, unknown	1062034	1061207
Hypothetical, unclassified, unknown	1062369	1062061
Hypothetical, unclassified, unknown	1062601	1062885
Hypothetical, unclassified, unknown	1062921	1063544
Hypothetical, unclassified, unknown	1065138	1065425
Secreted Factors (toxins, enzymes, algination		1066321
Hypothetical, unclassified, unknown	1068193	1068456
Hypothetical, unclassified, unknown	1071877	1071239
Hypothetical, unclassified, unknown	1072462	1072839
Chaperones & heat shock proteins	1073960	1074673
Hypothetical, unclassified, unknown	1082949	1083854
Hypothetical, unclassified, unknown	1090606	1090857
Adentation protection	1092498	1092025
Adaptation, protection Amino acid biosynthesis and metabolism	1093251	1094129
Hypothetical, unclassified, unknown	1095276	1096034
Nucleotide biosynthesis and metabolism	1096063	1096773
	1107000	1107761
Putative enzymes Hypothetical, unclassified, unknown	1113050	1112574
Three the tiest unclassified unknown	1123850	1123356
Hypothetical, unclassified, unknown	1125865	1125548
Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown	1126338	1125865
nypotnetical, unclassified, unknown		1137035
Biosynthesis of cofactors, prosthetic grou	1144862	1145200
Hypothetical, unclassified, unknown	1150470	1150721
Hypothetical, unclassified, unknown	1153637	1155547
Chaperones & heat shock proteins	1163660	1164022
Hypothetical, unclassified, unknown	1175614	1176375
Hypothetical, unclassified, unknown	11/3014	1110010

Hypothetical, unclassified, unknown	1176380	1176982
Hypothetical, unclassified, unknown	1176958	1177620
Hypothetical, unclassified, unknown	1186606	1186986
Two-component regulatory systems	1189172	1190380
Motility & Attachment	1194207	1195223
Motility & Attachment	1197390	1197833
Hypothetical, unclassified, unknown	1198551	1197838
Hypothetical, unclassified, unknown	1199946	1198750
Hypothetical, unclassified, unknown	1207875	1207540
Hypothetical, unclassified, unknown	1212571	1211888
Hypothetical, unclassified, unknown	1214502	1213195
Translation, post-translational modificatio	1215284	1215727
Biosynthesis of cofactors, prosthetic grou	1218181	1218933
Antibiotic resistance and susceptibility	1221691	1222098
Hypothetical, unclassified, unknown	1226278	1225757
Hypothetical, unclassified, unknown	1227302	1226427
Transcriptional regulators	1229344	1230219
Transcriptional regulators	1236644	1237546
Hypothetical, unclassified, unknown	1243118	1242750
Adaptation, protection	1245665	1245928
Hypothetical, unclassified, unknown	1249552	1249019
Nucleotide biosynthesis and metabolism	1251154	1249907
Nucleotide biosynthesis and metabolism	1254309	1251418
Two-component regulatory systems	1255042	1255752
Adaptation, protection	1257772	1257981
Hypothetical, unclassified, unknown	1258470	1258087
Amino acid biosynthesis and metabolism		1259291
Hypothetical, unclassified, unknown	1263378	1264190
Hypothetical, unclassified, unknown	1264919	1264191
Hypothetical, unclassified, unknown	1266111	1266782
Hypothetical, unclassified, unknown	1267282	1267602
Energy metabolism	1272796	1272200
Energy metabolism	1273298	1272807
Energy metabolism	1276608	1276117
Energy metabolism	1276784	1276617
Transport of small molecules	1284513	1285823
Hypothetical, unclassified, unknown	1294138	1294809
Hypothetical, unclassified, unknown	1303457	1303864
Hypothetical, unclassified, unknown	1303892	1304449
Hypothetical, unclassified, unknown	1305583	
Hypothetical, unclassified, unknown	1314321	
Hypothetical, unclassified, unknown	1317202	
Hypothetical, unclassified, unknown	1318150	
Amino acid biosynthesis and metabolisn		
Hypothetical, unclassified, unknown	1321000	
Transpiritional regulators	1326939	
Transcriptional regulators	1327024	
Putative enzymes Hypothetical, unclassified, unknown	1330467	
Inypotnetical, unclassified, unknown	1331517	
Hypothetical, unclassified, unknown	1334671	
Hypothetical, unclassified, unknown	1339082	
Antibiotic resistance and susceptibility		
Secreted Factors (toxins, enzymes, algi	IId (30/31/	100771

		1000115
Transcriptional regulators	1370092	1369418
Transcriptional regulators	1379168	1378500
Hypothetical, unclassified, unknown	1391277	1391861
Transcriptional regulators	1396731	1397180
Hypothetical, unclassified, unknown	1406459	1406752
Hypothetical, unclassified, unknown	1408999	1409274
Transcriptional regulators	1409949	1410476
Putative enzymes	1417500	1417961
Hypothetical, unclassified, unknown	1417965	1418738
Transcriptional regulators	1425754	1425140
Energy metabolism	1432037	1432927
Hypothetical, unclassified, unknown	1435493	1435825
Transcriptional regulators	1441547	1440639
Hypothetical, unclassified, unknown	1444451	1442904
Transport of small molecules	1456723	1455815
Hypothetical, unclassified, unknown	1462696	1463403
Hypothetical, unclassified, unknown	1463586	1463936
Hypothetical, unclassified, unknown	1464111	1464860
Hypothetical, unclassified, unknown	1467320	1466109
Hypothetical, unclassified, unknown	1467901	1467488
Hypothetical, unclassified, unknown	1468510	1468890
Hypothetical, unclassified, unknown	1470978	1470580
Hypothetical, unclassified, unknown	1474391	1474714
Transcriptional regulators	1475464	1476306
Hypothetical, unclassified, unknown	1479791	1479021
Hypothetical, unclassified, unknown	1483123	1483875
Hypothetical, unclassified, unknown	1483898	1485763
Hypothetical, unclassified, unknown	1486967	1486266
Hypothetical, unclassified, unknown	1489095	1486960
Biosynthesis of cofactors, prosthetic grou	1491913	1493055
Hypothetical, unclassified, unknown	1494959	1495492
Hypothetical, unclassified, unknown	1495635	1495997
Putative enzymes	1496920	1496087
Hypothetical, unclassified, unknown	1516433	1516687
Two-component regulatory systems	1518914	1519546
Hypothetical, unclassified, unknown	1519627	1519968
Hypothetical, unclassified, unknown	1526657	1526430
Carbon compound catabolism	1533238	1534278
Hypothetical, unclassified, unknown	1552641	1552997
Hypothetical, unclassified, unknown	1553112	1553675
Transcriptional regulators	1559122	
Adaptation, protection	1559254	
Hypothetical, unclassified, unknown	1572023	1572544
Motility & Attachment	1575290	1575559
Motility & Attachment	1583956	1584798
Two-component regulatory systems	1585640	1586014
Chemotaxis	1591286	1592176
Cell division	1592271	
Chemotaxis	1594087	1594566
Hypothetical, unclassified, unknown	1594597	1595004
Hypothetical, unclassified, unknown	1596889	
Hypothetical, unclassified, unknown	1599982	1599428

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Transport of small molecules	1602179	1602880
Transport of small molecules	1602877	1603548
Transport of small molecules	1603671	1604429
Hypothetical, unclassified, unknown	1604426	1604602
Energy metabolism	1605088	1607061
Energy metabolism	1607065	1607607
Energy metabolism	1607604	1608071
Hypothetical, unclassified, unknown	1615908	1614670
Hypothetical, unclassified, unknown	1617085	1615895
Hypothetical, unclassified, unknown	1619907	1620263
Transport of small molecules	1624715	1623864
Transcriptional regulators	1634492	1633842
Hypothetical, unclassified, unknown	1638639	1638379
Hypothetical, unclassified, unknown	1639794	1638652
Hypothetical, unclassified, unknown	1647046	1646537
Hypothetical, unclassified, unknown	1649555	1648629
Hypothetical, unclassified, unknown	1649928	1650308
Transcriptional regulators	1660727	1661386
Cell division	1665065	1665934
DNA replication, recombination, modification	1666025	1668409
DNA replication, recombination, modifica	t 1669989	1672034
Hypothetical, unclassified, unknown	1672080	1672406
Putative enzymes	1673204	1674352
Hypothetical, unclassified, unknown	1677559	1678407
Hypothetical, unclassified, unknown	1678590	1678261
Transport of small molecules	1678952	1678584
Hypothetical, unclassified, unknown	1684962	1684753
Energy metabolism	1689339	1687924
Energy metabolism	1694045	1693119
Hypothetical, unclassified, unknown	1696467	1697099
Hypothetical, unclassified, unknown	1697188	1697919
Hypothetical, unclassified, unknown	1697916	1698344
Hypothetical, unclassified, unknown	1704522	1704761
Hypothetical, unclassified, unknown	1709765	1709412
Hypothetical, unclassified, unknown	1712698	1712519 1721130
Energy metabolism	1720744	
Energy metabolism	1721124	1721492
Energy metabolism	1721496	
Energy metabolism	1723280	
Energy metabolism	1728416	
Energy metabolism	1730181	
Energy metabolism	1731347	
Hypothetical, unclassified, unknown	1734004	
Hypothetical, unclassified, unknown	1735063	
Hypothetical, unclassified, unknown	1735236	
Hypothetical, unclassified, unknown	1735706	
Hypothetical, unclassified, unknown	1736189	
Fatty acid and phospholipid metabolism	1753418	
Hypothetical, unclassified, unknown	1762433	
Transcriptional r gulators	1762928	
Putative enzymes	1765345	
Hypothetical, unclassified, unknown	1766285	176694

Hypothetical, unclassified, unknown	1766956	1767762
Transcriptional regulators	1773682	1774548
Transport of small molecules	1775945	1776034
Transport of small molecules i	1779877	1780428
Hypothetical, unclassified, unknown	1784108	1785016
Hypothetical, unclassified, unknown	1786888	1787166
Hypothetical, unclassified, unknown	1790879	1790472
Hypothetical, unclassified, unknown	1805218	1805724
Hypothetical, unclassified, unknown	1814995	1815135
Hypothetical, unclassified, unknown	1816352	1816858
Hypothetical, unclassified, unknown	1824969	1825430
Biosynthesis of cofactors, prosthetic grou	1826040	1825495
Hypothetical, unclassified, unknown	1826675	1826118
Hypothetical, unclassified, unknown	1827052	1826732
Amino acid biosynthesis and metabolism	1836367	1837227
Protein secretion/export apparatus	1841517	1840468
Protein secretion/export apparatus	1842302	1841514
Protein secretion/export apparatus	1845717	1845241
Protein secretion/export apparatus	1847227	1848093
Hypothetical, unclassified, unknown	1848707	1849072
Hypothetical, unclassified, unknown	1849077	1849406
Protein secretion/export apparatus	1851982	1852278
Protein secretion/export apparatus	1855862	1856299
Hypothetical, unclassified, unknown	1856308	1856553
Protein secretion/export apparatus	1862558	1862761
Protein secretion/export apparatus	1862764	1863021
Protein secretion/export apparatus	1863024	1863371
Protein secretion/export apparatus	1863799	1864137
Hypothetical, unclassified, unknown	1874967	1875767
Hypothetical, unclassified, unknown	1875849	1876580
Hypothetical, unclassified, unknown	1887297	1887058
Hypothetical, unclassified, unknown	1888186	1887698
Hypothetical, unclassified, unknown	1889173	1888985
Amino acid biosynthesis and metabolism	1891815	1890739
Amino acid biosynthesis and metabolism	1896630	1897247
Hypothetical, unclassified, unknown	1912756	1912217
Biosynthesis of cofactors, prosthetic grou	1917599	1918087
Transport of small molecules	1921174	1922226
Central intermediary metabolism	1926123	
Transport of small molecules	1931775	
Hypothetical, unclassified, unknown	1933632	
Energy metabolism	1937644	
Hypothetical, unclassified, unknown	1939583	
Hypothetical, unclassified, unknown	1942442	
Translation, post-translational modification		
Translation, post-translational modification	n 1944747	
Biosynthesis of cofactors, prosthetic grou	1947041	
Translation, post-translational modification	n 1956227	
DNA replication, recombination, modifica	1972959	
Nucleotide biosynthesis and metabolism	1973470	
Hypothetical, unclassified, unknown	1974627	
Transport of small molecules	1979941	
Transport of small molecules	1 1070041	

Hypothetical, unclassified, unknown	1984389	1985033
Hypothetical, unclassified, unknown	1989423	1989109
Hypothetical, unclassified, unknown	1993898	1993461
Hypothetical, unclassified, unknown	1995164	1994667
Hypothetical, unclassified, unknown	1998587	1998949
Hypothetical, unclassified, unknown	1999874	1999512
Hypothetical, unclassified, unknown	2004892	2004374
Hypothetical, unclassified, unknown	2007665	2008249
Hypothetical, unclassified, unknown	2012530	2012255
Hypothetical, unclassified, unknown	2015136	2014915
Transcriptional regulators	2019690	2018803
Transport of small molecules	2022398	2021712
Hypothetical, unclassified, unknown	2028454	2028981
Fatty acid and phospholipid metabolism	2031466	2031705
Hypothetical, unclassified, unknown	2034857	2034066
Hypothetical, unclassified, unknown	2052941	2053264
Transport of small molecules	2053277	2053675
Energy metabolism	2054223	2053672
Transcriptional regulators	2054309	2054842
Hypothetical, unclassified, unknown	2062401	2061664
Hypothetical, unclassified, unknown	2065545	2064853
Hypothetical, unclassified, unknown		2065493
Hypothetical, unclassified, unknown	2066767	2065493
Hypothetical, unclassified, unknown	2067955	2067961
Hypothetical, unclassified, unknown	2068728	2071173
Secreted Factors (toxins, enzymes, algination		2071697
Secreted Factors (toxins, enzymes, algination		2076958
Secreted Factors (toxins, enzymes, alginates)	2076311	
Transcriptional regulators	2085426	2084476
Transcriptional regulators	2085929	2085423
Hypothetical, unclassified, unknown	2088034	2086808 2091490
Hypothetical, unclassified, unknown	2091837	2103770
Hypothetical, unclassified, unknown	2103294	2103770
Hypothetical, unclassified, unknown	2103770	2104090
Translation, post-translational modification	h 2109511	2109558
Hypothetical, unclassified, unknown	2109854	2118097
Hypothetical, unclassified, unknown	2117897	
Hypothetical, unclassified, unknown	2118585	2118893
Hypothetical, unclassified, unknown	2118926	
Hypothetical, unclassified, unknown	2122222	
Hypothetical, unclassified, unknown	2137785	
Hypothetical, unclassified, unknown	2138598	
Hypothetical, unclassified, unknown	2141002	
Hypothetical, unclassified, unknown	2141487	
Hypothetical, unclassified, unknown	2145894	
Hypothetical, unclassified, unknown	2146609	
Hypothetical, unclassified, unknown	2148854	
Hypothetical, unclassified, unknown	2150364	
Hypothetical, unclassified, unknown	2150524	
Hypothetical, unclassified, unknown	2157968	
Transcriptional regulators	2164548	
Two-component regulatory systems	2165876	
Biosynthesis of cofactors, prosthetic gro	u 2171865	2171936

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Biosynthesis of cofactors, prosthetic grou	2171989	2172903
Biosynthesis of cofactors, prosthetic group	2173662	2173940
Hypothetical, unclassified, unknown	2181744	2181181
Hypothetical, unclassified, unknown	2182097	2181741
Chaperones & heat shock proteins	2182394	2182116
Fatty acid and phospholipid metabolism	2187065	2188246
Hypothetical, unclassified, unknown	2188459	2189883
Carbon compound catabolism	2196132	2195494
Transcriptional regulators	2198891	2199694
Putative enzymes	2203446	2202649
Fatty acid and phospholipid metabolism	2206353	2205190
Transcriptional regulators	2206806	2206402
Hypothetical, unclassified, unknown	2206999	2207928
Hypothetical, unclassified, unknown	2213539	2213315
Hypothetical, unclassified, unknown	2219099	2218098
Hypothetical, unclassified, unknown	2220275	2220574
Hypothetical, unclassified, unknown	2221157	2220903
Hypothetical, unclassified, unknown	2223804	2224478
Hypothetical, unclassified, unknown	2227541	2229001
Transport of small molecules	2234080	2235309
Transcriptional regulators	2244995	2245948
Central intermediary metabolism	2246456	2245986
Transport of small molecules	2256704	2257720
Putative enzymes	2259478	2260659
Hypothetical, unclassified, unknown	2265764	2265126
Translation, post-translational modification	2272460	2274568
Transport of small molecules	2277552	2278982
Hypothetical, unclassified, unknown	2278982	2279794
Hypothetical, unclassified, unknown	2281578	2279917
Hypothetical, unclassified, unknown	2290335	2289085
Hypothetical, unclassified, unknown	2297072	2297920
Hypothetical, unclassified, unknown	2300676	2301755
Transport of small molecules	2303022	2304215
Hypothetical, unclassified, unknown	2306627	2305782
Carbon compound catabolism	2307957	2309432 2313789
Hypothetical, unclassified, unknown	2312899	2315690
Biosynthesis of cofactors, prosthetic grou	2314512	2317403
Putative enzymes	2316708	
Hypothetical, unclassified, unknown	2318624 2322071	2321130
Hypothetical, unclassified, unknown		
DNA replication, recombination, modification	2329348 2332059	
Putative enzymes	2332820	
Hypothetical, unclassified, unknown	2335172	2336104
Transcriptional regulators	2339987	
Hypothetical, unclassified, unknown	2339967	
Hypothetical, unclassified, unknown	2352430	
Hypothetical, unclassified, unknown	2356713	
Putative enzymes	2358024	
Hypothetical, unclassified, unknown	2361706	
Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown	2364816	
Hypothetical, unclassified, unknown	2377476	
inypothetical, unclassified, unknown		

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Hypothetical, unclassified, unknown	2381778	2381473
Hypothetical, unclassified, unknown	2390255	2390620
Hypothetical, unclassified, unknown	2390949	
Hypothetical, unclassified, unknown	2393424	2393633
Hypothetical, unclassified, unknown	2393708	2394178
Hypothetical, unclassified, unknown	2396252	2395944
Hypothetical, unclassified, unknown	2396883	2396536
Hypothetical, unclassified, unknown	2404655	2404386
Hypothetical, unclassified, unknown	2405233	2404949
Hypothetical, unclassified, unknown	2405739	2405230
Hypothetical, unclassified, unknown	2405993	2406877
Hypothetical, unclassified, unknown	2406961	2407131
Hypothetical, unclassified, unknown	2407236	2407661
Hypothetical, unclassified, unknown	2409837	2410181
Hypothetical, unclassified, unknown	2411709	2412122
Transcriptional regulators	2415661	2416245
Hypothetical, unclassified, unknown	2416376	2417413
Hypothetical, unclassified, unknown	2424400	2423924
Hypothetical, unclassified, unknown	2427017	2425497
Hypothetical, unclassified, unknown	2430170	2431129
Transport of small molecules	2433748	2435070
Transport of small molecules	2441555	2440347
Transcriptional regulators	2441771	2442691
Hypothetical, unclassified, unknown	2443161	2444366
Hypothetical, unclassified, unknown	2445533	2444886
Hypothetical, unclassified, unknown	2446564	2445545
Hypothetical, unclassified, unknown	2447325	2446597
Hypothetical, unclassified, unknown	2447989	2447573
Hypothetical, unclassified, unknown	2448533	2448033
Transcriptional regulators	2449545	2448568
Hypothetical, unclassified, unknown	2450765	2449554
Hypothetical, unclassified, unknown	2451707	2452426
Transport of small molecules	2457510	2458280
Hypothetical, unclassified, unknown	2468032	. 2469099
Hypothetical, unclassified, unknown	2472104	2472409
Hypothetical, unclassified, unknown	2479130	2478312
Amino acid biosynthesis and metabolism	2480844	
Secreted Factors (toxins, enzymes, algin	a 2485471	
Transcriptional regulators	2487293	
Hypothetical, unclassified, unknown	2488950	
Hypothetical, unclassified, unknown	2508775	
Hypothetical, unclassified, unknown	2510622	
Hypothetical, unclassified, unknown	2512511	2513182
Hypothetical, unclassified, unknown	2523239	
Hypothetical, unclassified, unknown	2524201	
Transport of small molecules	2525052	
Transport of small molecules	2525846	
Energy metabolism	2527657	
Putative enzymes	2529467	
Hypothetical, unclassified, unknown	2540082	
Hypothetical, unclassified, unknown	2549748	
Transcriptional regulators	2553965	2554858
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Transport of small molecules 2571691 2570855 Hypothetical, unclassified, unknown 2573365 2572805 Hypothetical, unclassified, unknown 2579542 2580882 Transport of small molecules 2582097 2583407 Carbon compound catabolism 2587906 2589414 Hypothetical, unclassified, unknown 2593330 2594547 Hypothetical, unclassified, unknown 2597869 2598522 Hypothetical, unclassified, unknown 2617019 2617519 Hypothetical, unclassified, unknown 26177529 261795- Hypothetical, unclassified, unknown 2617529 261795- Hypothetical, unclassified, unknown 2623284 262385 Hypothetical, unclassified, unknown 2623284 262385 Hypothetical, unclassified, unknown 2635971 263505 Transcriptional regulators 2635971 263505 Transport of small molecules 2645303 264672 Hypothetical, unclassified, unknown 2689240 268956 Hypothetical, unclassified, unknown 2694544 269378
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Transport of small molecules Hypothetical, unclassified, unknown Putative enzymes Hypothetical, unclassified, unknown
Transport of small molecules Hypothetical, unclassified, unknown
Hypothetical, unclassified, unknown Putative enzymes Puta
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Putative enzymes Hypothetical, unclassified, unknown 2694763 269454 Hypothetical, unclassified, unknown 2701205 270206 Hypothetical, unclassified, unknown 2705772 270608 Hypothetical, unclassified, unknown 2723221 272275 Hypothetical, unclassified, unknown 2724222 272330 Hypothetical, unclassified, unknown 2724484 272472 Hypothetical, unclassified, unknown 2730520 272997 Hypothetical, unclassified, unknown 2732965 273253 Hypothetical, unclassified, unknown 2738840 273971 Amino acid biosynthesis and metabolism 2740882 273976 Amino acid biosynthesis and metabolism 2740882 273976 Amino acid biosynthesis and metabolism 274072 274668 Hypothetical, unclassified, unknown 2753464 275286 Hypothetical, unclassified, unknown 2755724 275625 Hypothetical, unclassified, unknown 2756308 275664 Hypothetical, unclassified, unknown 2760086 275948 Hypothetical, unclassified, unknown 2760086 275948 Hypothetical, unclassified, unknown 2760618 276032
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Hypothetical unclassified unknown 27613501 276087
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Hypothetical, unclassified, unknown 2781450 278092
Transcriptional regulators 2786355 278535
Transcriptional regulators 2787885 278697
Central intermediary metabolism 2791219 279186
Hypothetical, unclassified, unknown 2791905 279281
Putative enzymes 2794132 279279
Hypothetical, unclassified, unknown 2803344 280362
Hypothetical, unclassified, unknown 2804131 280385
Hypothetical, unclassified, unknown 2805916 280629
Putative enzymes 2807368 280634
Transcriptional regulators 2807468 28085
Hypothetical, unclassified, unknown 2815281 281476
Transport of small molecules 2817448 28186
Hypothetical unclassified unknown 2818885 28187 Hypothetical unclassified unknown 2822321 282170
Hypothetical, unclassified, unknown 2822321 282170

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Carbon compound catabolism	2825590	2824658
Carbon compound catabolism	2833129	2832368
Carbon compound catabolism	2834689	2834201
Transport of small molecules	2841965	2840511
Fatty acid and phospholipid metabolism	2865104	2864169
Hypothetical, unclassified, unknown	2866199	2865747
Hypothetical, unclassified, unknown	2867505	2866192
Hypothetical, unclassified, unknown	2876409	2875696
Hypothetical, unclassified, unknown	2880519	2881562
Transcriptional regulators	2883156	2884088
Putative enzymes	2885332	2884205
Putative enzymes	2886551	2885361
Putative enzymes	2887336	2886569
Transcriptional regulators	2913921	2914358
Fatty acid and phospholipid metabolism	2923926	2923366
Transcriptional regulators	2934387	2933581
Hypothetical, unclassified, unknown	2945263	2945868
Hypothetical, unclassified, unknown	2948581	2948976
Hypothetical, unclassified, unknown	2948973	2949332
Hypothetical, unclassified, unknown	2949332	2949637
Hypothetical, unclassified, unknown	2949634	2949969
Translation, post-translational modificatio	n 2954695	2953415
Chaperones & heat shock proteins	2956778	2956152
Cell division	2959239	2956804
Translation, post-translational modificatio	n 2960455	2961135
Translation, post-translational modificatio	n 2962002	2962220
Hypothetical, unclassified, unknown	2964842	2964606
Transcription, RNA processing and degra	2969986	2971113
Nucleotide biosynthesis and metabolism	2972698	2974068
Energy metabolism	2983204	2983881
Energy metabolism	2986242	2987588
Energy metabolism	2992001	2992501
Energy metabolism	2992547	2992855
Hypothetical, unclassified, unknown	3008323	3008009
Hypothetical, unclassified, unknown	3012536	3012279
Biosynthesis of cofactors, prosthetic group	3015581	3015937
Hypothetical, unclassified, unknown	3016245	3016598
Hypothetical, unclassified, unknown	3016883	
Protein secretion/export apparatus	3020928	
Protein secretion/export apparatus	3021338	
Protein secretion/export apparatus	3021741	
Transport of small molecules	3025507	
Transcriptional regulators •	3028074	
Amino acid biosynthesis and metabolism	3031397	
Hypothetical, unclassified, unknown	3042501	
Related to phage, transposon, or plasmi	d 3044765	
Energy metabolism	3047969	
Hypothetical, unclassified, unknown	3050611	
Hypothetical, unclassified, unknown	3057375	
Hypothetical, unclassified, unknown	3060659	
Energy metabolism	3070365	
Hypothetical, unclassified, unknown	3073731	3074417

Hypothetical, unclassified, unknown	3075217	3074579
Hypothetical, unclassified, unknown	3075410	3075889
Hypothetical, unclassified, unknown	3075921	3076313
Hypothetical, unclassified, unknown	3076343	3076621
Central intermediary metabolism	3079196	3079834
Hypothetical, unclassified, unknown	3089612	3088659
Hypothetical, unclassified, unknown	3090107	3089643
Hypothetical, unclassified, unknown	. 3094184	3093657
Hypothetical, unclassified, unknown	3096051	3094756
Hypothetical, unclassified, unknown	3098978	3098625
Hypothetical, unclassified, unknown	3099729	3099472
DNA replication, recombination, modificat	3100111	3099809
Translation, post-translational modification	3102493	3100115
Translation, post-translational modification	n 3103544	3102528
Translation, post-translational modification	n 3103998	3103642
Translation, post-translational modification	3104216	3104022
Translation, post-translational modification	3104829	3104278
Translation, post-translational modification	n 3106751	3104829
DNA replication, recombination, modificat	3110900	. 3111613
Hypothetical, unclassified, unknown	3114818	3115192
Hypothetical, unclassified, unknown	3117610	3117176
Hypothetical, unclassified, unknown	3119707	3119393
Hypothetical, unclassified, unknown	3122264	3121920
Hypothetical, unclassified, unknown	3122585	3122376
Putative enzymes	3126251	3127219
Hypothetical, unclassified, unknown	3127225	3127707
Hypothetical, unclassified, unknown	3128269	3127859
Hypothetical, unclassified, unknown	3132815	3132228
Hypothetical, unclassified, unknown	3133257	3132820
Hypothetical, unclassified, unknown	3137849	3138193
Hypothetical, unclassified, unknown	3138190	3138531
Hypothetical, unclassified, unknown	3139010	3139669
Hypothetical, unclassified, unknown	3141718	3142275
Hypothetical, unclassified, unknown	3142284	3142502
Hypothetical, unclassified, unknown	3142617	3143084
Hypothetical, unclassified, unknown	3149318	3148722
Hypothetical, unclassified, unknown	3152201	3150885
Hypothetical, unclassified, unknown	3155074	3154592
Hypothetical, unclassified, unknown	3156502	
Hypothetical, unclassified, unknown	3157563	
Hypothetical, unclassified, unknown	3158925	
Hypothetical, unclassified, unknown	3160320	
Hypothetical, unclassified, unknown	3162215	
Hypothetical, unclassified, unknown	3162578	
Transport of small molecules	3165541	3164762
Hypothetical, unclassified, unknown	3173174	
Hypothetical, unclassified, unknown	3173243	
Hypothetical, unclassified, unknown	3180951	
Hypothetical, unclassified, unknown	3182399	
Hypothetical, unclassified, unknown	3184001	
Adaptation, protection	3185816	
Hypothetical, unclassified, unknown	3192748	3193518

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Putative enzymes	3197641	3198987
Hypothetical, unclassified, unknown	3200552	3200319
Translation, post-translational modification	3205079	3204513
Hypothetical, unclassified, unknown	3206252	3205122
Membrane proteins	3206914	3207165
Hypothetical, unclassified, unknown	3208260	3207289
Transcription, RNA processing and degra	3212524	3213030
Secreted Factors (toxins, enzymes, algina	3215422	3216288
Hypothetical, unclassified, unknown	3221205	3221564
Hypothetical, unclassified, unknown	3228336	3227383
Nucleotide biosynthesis and metabolism	3230181	3229483
Transcriptional regulators	3231171	3230278
Transcriptional regulators	3232771	3231881
Hypothetical, unclassified, unknown	3235793	3235960
Hypothetical, unclassified, unknown	3249630	3249208
Hypothetical, unclassified, unknown	3253679	3253311
Hypothetical, unclassified, unknown	· 3255765	3255406
Hypothetical, unclassified, unknown	3265210	3264641
Hypothetical, unclassified, unknown	3271692	3270826
Hypothetical, unclassified, unknown	3272405	3271812
Putative enzymes	3277408	3278577
Hypothetical, unclassified, unknown	3284597	3283374
Hypothetical, unclassified, unknown	3291172	3290693
Hypothetical, unclassified, unknown	3291282	3291863
Hypothetical, unclassified, unknown	3291959	3292267
Putative enzymes	3297117	3295978
Putative enzymes	3308390	3309337
Energy metabolism	3311720	3310791
Energy metabolism	3312469	3311720
Energy metabolism	3312790	3314445
Motility & Attachment	3320029	3319673
DNA replication, recombination, modificat	3321049	3320063
Nucleotide biosynthesis and metabolism	3321674	3321042
Hypothetical, unclassified, unknown	3322752	3321703
Fatty acid and phospholipid metabolism	3325182	3324946
Fatty acid and phospholipid metabolism	3326121	3325378
Fatty acid and phospholipid metabolism	3327082	3326144
Translation, post-translational modification	n 3328384	
Hypothetical, unclassified, unknown	3328934	
Transcription, RNA processing and degra		
Cell wall / LPS / capsule	3337230	
Translation, post-translational modification	ի 3337691	
Cell wall / LPS / capsule	3338455	
Hypothetical, unclassified, unknown	3338640	
Cell wall / LPS / capsule	3339676	
Hypothetical, unclassified, unknown	3340116	
Transport of small molecules	3340748	
Hypothetical, unclassified, unknown	3343177	
Hypothetical, unclassified, unknown	3345099	
Transport of small molecules	3345795	
Hypothetical, unclassified, unknown	3347038	
Hypothetical, unclassified, unknown	3346976	3347740

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Nucleotide biosynthesis and metabolism	3350231	3348837
Hypothetical, unclassified, unknown	3350637	3350410
Energy metabolism	3354171	3353497
Putative enzymes	3360653	3359268
Nucleotide biosynthesis and metabolism	3365743	3365006
Hypothetical, unclassified, unknown	3369268	3369035
DNA replication, recombination, modificat	3372705	3370099
Hypothetical, unclassified, unknown	3373170	3372796
Hypothetical, unclassified, unknown	3378511	3378948
Hypothetical, unclassified, unknown	3383947	3384333
Hypothetical, unclassified, unknown	3385183	3384377
Putative enzymes	3387828	3386269
Biosynthesis of cofactors, prosthetic grou	3394087	3394683
Hypothetical, unclassified, unknown	3397373	3397095
Hypothetical, unclassified, unknown	3398716	3399648
Hypothetical, unclassified, unknown	3403811	3404140
Hypothetical, unclassified, unknown	3404144	3404524
Hypothetical, unclassified, unknown	3404538	3404861
Hypothetical, unclassified, unknown	3409952	3409608
Translation, post-translational modification	3414400	3414612
Hypothetical, unclassified, unknown	3416066	3415785
Transcriptional regulators	3436429	3435986
Hypothetical, unclassified, unknown	3457909	3456542
Hypothetical, unclassified, unknown	3464151	3463888
Hypothetical, unclassified, unknown	3466959	3466072
Hypothetical, unclassified, unknown	3467084	3468049
Hypothetical, unclassified, unknown	3473017	3474135
Protein secretion/export apparatus	3476479	3475955
Protein secretion/export apparatus	3477629	3476481
Protein secretion/export apparatus	3480238	3479720
Protein secretion/export apparatus	3483421	3481913
Hypothetical, unclassified, unknown	3491410	3490751
Fatty acid and phospholipid metabolism	3493572	3492700
Amino acid biosynthesis and metabolism	3500597	3499485
Hypothetical, unclassified, unknown	3506241	3505864
Hypothetical, unclassified, unknown	3524489	3524160 3527428
Hypothetical, unclassified, unknown	3527733	
Hypothetical, unclassified, unknown	3528349	3528230
Cell wall / LPS / capsule	3529446	
Cell wall / LPS / capsule	3530457	
Cell wall / LPS / capsule	3531707	
Cell wall / LPS / capsule	3532814	
Cell wall / LPS / capsule	3533932	
Cell wall / LPS / capsule	3535080	
Amino acid biosynthesis and metabolism	3535970	
Amino acid biosynthesis and metabolism	3536578	
Cell wall / LPS / capsule	3537810 3539123	
Cell wall / LPS / capsule	3540206	
Cell wall / LPS / capsule	3540208	
Cell wall / LPS / capsule	3542670	
Cell wall / LPS / capsule	3543689	
Cell wall / LPS / capsule	1 3343009	1 55-121 55

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Cell wall / LPS / capsule	3545073	3543763
Cell wall / LPS / capsule	3546926	3545880
DNA replication, recombination, modificat	3547972	3547688
Translation, post-translational modification	3549788	3548109
Nucleotide biosynthesis and metabolism	3550745	3550056
Biosynthesis of cofactors, prosthetic grou	3556338	3555253
DNA replication, recombination, modificat	3559197	3556426
Biosynthesis of cofactors, prosthetic grou	3562105	3562803
Hypothetical, unclassified, unknown	3569012	3568635
Carbon compound catabolism	3571602	3570940
Hypothetical, unclassified, unknown	3575696	3574845
Carbon compound catabolism	3587432	3588436
Hypothetical, unclassified, unknown	3593732	3594031
Hypothetical, unclassified, unknown	3594207	3594569
Hypothetical, unclassified, unknown	3597318	3597797
Transport of small molecules	3600453	3601598
Transcriptional regulators	3609075	3609839
Chaperones & heat shock proteins	3614303	3614866
Hypothetical, unclassified, unknown	3618466	3617342
Putative enzymes	3619618	3618992
Hypothetical, unclassified, unknown	3624836	3625057
Cell wall / LPS / capsule	3630604	3629666
Cell division	3632429	3632683
Transcription, RNA processing and degra		3633422
Transcriptional regulators	3636256	3635540
Hypothetical, unclassified, unknown	3641232	3641810
Transcriptional regulators	3648065	3647754
Adaptation, protection	3653666	3653875
Hypothetical, unclassified, unknown	3668522	3667923
Hypothetical, unclassified, unknown	3668473	3668760
Hypothetical, unclassified, unknown	3669168	3668839 3670758
Hypothetical, unclassified, unknown	3671057	3673007
Transport of small molecules	3674323	3674569
Hypothetical, unclassified, unknown	3675159	3680460
Hypothetical, unclassified, unknown	3679945	3680464
Hypothetical, unclassified, unknown	3680967	3681460
Hypothetical, unclassified, unknown	3681047	
Hypothetical, unclassified, unknown	3684716	
Hypothetical, unclassified, unknown	3685761	
Hypothetical, unclassified, unknown	3695480	
Hypothetical, unclassified, unknown	3700315	·
Hypothetical, unclassified, unknown	3710224	
Putative enzymes	3715804	
Transport of small molecules	3716807	
Transport of small molecules	3717604	
Hypothetical, unclassified, unknown	3719328	
Hypothetical, unclassified, unknown	3720122	
Hypothetical, unclassified, unknown	3723444	
Translation, post-translational modification	oh 3730075	
Putative enzymes	3740104	
Hypothetical, unclassified, unknown	3742264	
Fatty acid and phospholipid metabolism	3743699	3743938

Hypothetical, unclassified, unknown	3747455	3747165
Transcriptional regulators	3752477	3752043
Hypothetical, unclassified, unknown	3759680	3759375
Chemotaxis	3760819	3759995
Hypothetical, unclassified, unknown	3762803	3763126
Hypothetical, unclassified, unknown	3763680	3764471
Hypothetical, unclassified, unknown	3765086	3764475
Secreted Factors (toxins, enzymes, algina	3772560	3771502
Hypothetical, unclassified, unknown	3778265	3778603
Putative enzymes	3778703	3779368
Hypothetical, unclassified, unknown	3779929	3780075
Hypothetical, unclassified, unknown	3780127	3780312
Hypothetical, unclassified, unknown	3787478	3787020
Transport of small molecules	3790985	3790149
Hypothetical, unclassified, unknown	3794116	3793814
Energy metabolism	3801103	3801930
Energy metabolism	3801947	3802483
Energy metabolism	3803342	3802566
Hypothetical, unclassified, unknown	3808802	3808317
Transport of small molecules	3814574	3813957
Hypothetical, unclassified, unknown	3820005	3820271
Hypothetical, unclassified, unknown	3820307	3820891
Energy metabolism	3823515	3822514
Hypothetical, unclassified, unknown	3840747	3840358
Transcriptional regulators	3840843	3841736
Related to phage, transposon, or plasmid	3843289	3842273
Hypothetical, unclassified, unknown	3844104	3843652
Biosynthesis of cofactors, prosthetic grou	3845774	3846334
Biosynthesis of cofactors, prosthetic grou	3846336	3846707
Transport of small molecules	3849582	3848794
Hypothetical, unclassified, unknown	3850751	3849603
Hypothetical, unclassified, unknown	3851800	3850829
Hypothetical, unclassified, unknown	3852512	3851919
Adaptation, protection	3856130	3855492
Hypothetical, unclassified, unknown	3856336	3856545
Putative enzymes	3867706	3869463
Hypothetical, unclassified, unknown	3882979	3883437
Hypothetical, unclassified, unknown	3885710	3886306
Transcriptional regulators	3890649	
Translation, post-translational modification	h 3895323	
Hypothetical, unclassified, unknown	3906390	
Hypothetical, unclassified, unknown	3907267	
Hypothetical, unclassified, unknown	3910738	3911772
Hypothetical, unclassified, unknown	3912409	3913131
DNA replication, recombination, modifica	3913128	3913766
Hypothetical, unclassified, unknown	3913875	3914054
Hypothetical, unclassified, unknown	3918468	3918250
Hypothetical, unclassified, unknown	3918787	
Hypothetical, unclassified, unknown	3922072	
Transport of small molecules	3928333	
Hypothetical, unclassified, unknown	3936836	
Hypothetical, unclassified, unknown	3937431	1
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Transport of small molecules	3943806	3942649
Transcription, RNA processing and degra	3948137	3948811
Hypothetical, unclassified, unknown	3949852	3950073
Hypothetical, unclassified, unknown	. 3952386	3952060
Secreted Factors (toxins, enzymes, algin	3965841	3967010
Secreted Factors (toxins, enzymes, algina	3977183	3977833
Hypothetical, unclassified, unknown	3986879	3987292
Hypothetical, unclassified, unknown	3997821	3998114
Carbon compound catabolism	4003600	4002107
Hypothetical, unclassified, unknown	4004782	4004958
Hypothetical, unclassified, unknown	4007506	4008036
Hypothetical, unclassified, unknown	4010326	4009541
Carbon compound catabolism	4023176	4021971
Hypothetical, unclassified, unknown	4035757	4035605
Hypothetical, unclassified, unknown	4036020	4035757
Hypothetical, unclassified, unknown	4039173	4040099
Hypothetical, unclassified, unknown	4040819	4040103
Transport of small molecules	4043060	4043830
Hypothetical, unclassified, unknown	4045159	4045569
Hypothetical, unclassified, unknown	4045588	4045809
Hypothetical, unclassified, unknown	4051557	4051096
DNA replication, recombination, modification	4052603	4051563
Hypothetical, unclassified, unknown	4062898	4062425
Hypothetical, unclassified, unknown	4067294	4067542
Hypothetical, unclassified, unknown	4068307	4067603
Hypothetical, unclassified, unknown	4068611	4068327
Carbon compound catabolism	4069965	4068676
Cell wall / LPS / capsule	4070856	4070011
Nucleotide biosynthesis and metabolism	4072487	4070859
Hypothetical, unclassified, unknown	4073986	4072658
Fatty acid and phospholipid metabolism	4075006	4074056
DNA replication, recombination, modifica	4078677	4075156
Cell wall / LPS / capsule	4082180	4081044
Cell wall / LPS / capsule	4082960	4082184
Fatty acid and phospholipid metabolism	4083397	4082957
C II wall / LPS / capsule	4084504	4083443
Transport of small molecules	4085010	
Transport of small molecules	4087454	
Biosynthesis of cofactors, prosthetic group	4090093	
Fatty acid and phospholipid metabolism	4090905	
Cell wall / LPS / capsule	4091654	
Translation, post-translational modification	oh 4092227	
Nucleotide biosynthesis and metabolism	4092967	
Translation, post-translational modification	oh 4094035	
Translation, post-translational modification	on 4094906	
Translation, post-translational modification	oh 4095171	
Hypothetical, unclassified, unknown	4102767	
Hypothetical, unclassified, unknown	4103731	
Cell wall / LPS / capsule	4104744	
Transport of small molecules	4111080	
Hypothetical, unclassified, unknown	4114932	
Transcriptional regulators	4120468	4121100

		1100000
Hypothetical, unclassified, unknown	4123955	4123260
Hypothetical, unclassified, unknown	4126089	4125742
Hypothetical, unclassified, unknown	4126843	4126163
Hypothetical, unclassified, unknown	4130598	4130942
Hypothetical, unclassified, unknown	4135972	4135451
Translation, post-translational modification	1 4143664	4142569
Chemotaxis	4148251	4145942
Hypothetical, unclassified, unknown	4165879	4165718
DNA replication, recombination, modificat	4172484	4170769
Hypothetical, unclassified, unknown	4173067	4172528
Hypothetical, unclassified, unknown	4182018	4181377
Hypothetical, unclassified, unknown	4182769	4182074
Hypothetical, unclassified, unknown	4183709	4184938
Translation, post-translational modificatio	n 4195357	4195007
Transcription, RNA processing and degra	4196157	4195399
Transcription, RNA processing and degra	4196691	4196164
Translation, post-translational modificatio	n 4196958	4196707
Protein secretion/export apparatus	4198541	4197168
Hypothetical, unclassified, unknown	4204736	4204542
Hypothetical, unclassified, unknown	4205906	4205295
Hypothetical, unclassified, unknown	4206664	4207164
Putative enzymes	4209255	4210277
Hypothetical, unclassified, unknown	4221796	4221212
Hypothetical, unclassified, unknown	4224115	4223567
Nucleotide biosynthesis and metabolism	4227236	4225659
Hypothetical, unclassified, unknown	4231070	4232227
Transcriptional regulators	4234274	4235182
DNA replication, recombination, modifica	4235219	4236598
Transcriptional regulators	4242294	4241341
Hypothetical, unclassified, unknown	4243651	4243079
Hypothetical, unclassified, unknown	4244184	4243708
Hypothetical, unclassified, unknown	4244875	4245723
Hypothetical, unclassified, unknown	4245809	4246204
Hypothetical, unclassified, unknown	4255323	4254736
Hypothetical, unclassified, unknown	4260396	4259254
Hypothetical, unclassified, unknown	4263492	4262377
Motility & Attachment	4265287	4264529
Hypothetical, unclassified, unknown	4266444	
Nucleotide biosynthesis and metabolism	4266900	
Hypothetical, unclassified, unknown	4267344	
Energy metabolism	4267709	
Chaperones & heat shock proteins	4269575	
Chaperones & heat shock proteins	4270139	
Biosynthesis of cofactors, prosthetic gro	u 4270470	
Biosynthesis of cofactors, prosthetic gro	u 4270884	
Hypothetical, unclassified, unknown	4272655	
Protein secretion/export apparatus	4278946	
Hypothetical, unclassified, unknown	4279344	
Hypothetical, unclassified, unknown	4285483	
Hypothetical, unclassified, unknown	4286594	
Hypothetical, unclassified, unknown	4287709	
Hypothetical, unclassified, unknown	4290866	4291234

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Translation, post-translational modification	4291355	4294207
Hypothetical, unclassified, unknown	4294604	4294254
Hypothetical, unclassified, unknown	4302040	4303050
Hypothetical, unclassified, unknown	4305063	4305425
Hypothetical, unclassified, unknown	4311861	4310950
Hypothetical, unclassified, unknown	4312702	4311950
Hypothetical, unclassified, unknown	4314794	4314480
Hypothetical, unclassified, unknown	4316037	4315555
Hypothetical, unclassified, unknown	4316824	4316108
Putative enzymes	4318258	4318905
DNA replication, recombination, modificat	4330320	4330895
Hypothetical, unclassified, unknown	4331451	4332461
Hypothetical, unclassified, unknown	4332652	4333035
Transport of small molecules	4343527	4342121
Hypothetical, unclassified, unknown	4350352	4350738
Hypothetical, unclassified, unknown	4351594	4352493
Transport of small molecules	4354543	4355265
Transport of small molecules	4356200	4356862
Transport of small molecules	4356875	4358038
Hypothetical, unclassified, unknown	4359074	4358166
Hypothetical, unclassified, unknown	4373937	4374332
Hypothetical, unclassified, unknown	4374329	4374856
Hypothetical, unclassified, unknown	4374849	4375232
Hypothetical, unclassified, unknown	4382015	4381500
Biosynthesis of cofactors, prosthetic grou	4386351	4385899
Biosynthesis of cofactors, prosthetic grou	4386607	4386356
Biosynthesis of cofactors, prosthetic grou	4387086	4386604
Transport of small molecules	4414949	4414131
DNA replication, recombination, modifica	4418302	4418583
Hypothetical, unclassified, unknown	4439376	4439783
Hypothetical, unclassified, unknown	4442452	4442868
Transcriptional regulators	4444977	4445486
Hypothetical, unclassified, unknown	4445998	4446390
Hypothetical, unclassified, unknown	4447132	4448217
Transcriptional regulators	4453182	4452535
Biosynthesis of cofactors, prosthetic grou	4457361	4458644
Hypothetical, unclassified, unknown	4459749	
Hypothetical, unclassified, unknown	4461387	4462409
Hypothetical, unclassified, unknown	4462399	
Translation, post-translational modification	n 4463903	4465438
Hypothetical, unclassified, unknown	4466753	4466322
Translation, post-translational modification		
Hypothetical, unclassified, unknown	4469612	
DNA replication, recombination, modifica		
Hypothetical, unclassified, unknown	4471402	
Related to phage, transposon, or plasmic		
Biosynthesis of cofactors, prosthetic ground		
Hypothetical, unclassified, unknown	4478907	
Cell wall / LPS / capsule	4483363	
Hypothetical, unclassified, unknown	4486179	
Hypothetical, unclassified, unknown	4486846	
Putative enzymes	4488409	
rulauve enzymes		

Secreted Factors (toxins, enzymes, algina decreted Factors) decreted Factors (toxins, enzymes, a		474270F:	4714283
Secreted Factors (toxins, enzymes, algina) 4714825 4716042 Secreted Factors (toxins, enzymes, algina) 4718566 4719392 Secreted Factors (toxins, enzymes, algina) 4718456 4719392 Secreted Factors (toxins, enzymes, algina) 4724034 4722850 Hypothetical, unclassified, unknown 4724034 4722850 Transport of small molecules 4744818 4746123 DNA replication, recombination, modifical 4744818 4745123 Translation, post-translational modification 47564378 4753989 Translation, post-translational modification 4756472 4756482 Translation, post-translational modification 47566742 4756491 Translation, post-translational modification 4756847 4756978 Translation, post-translational modification 4758866 4758452 Translation, post-translational modification 4758866 4758452 Translation, post-translational modification 4759066 4758890 Translation, post-translational modification 4759069 4759069 Translation, post-translational modification 4760467 47599	Secreted Factors (toxins, enzymes, aigina		
Secreted Factors (toxins, enzymes, algina de 1718556 de 1719392) Secreted Factors (toxins, enzymes, algina de 1719418 de 1720062 de	Secreted Factors (toxins, enzymes, algina		
Secreted Factors (toxins, enzymes, algina 4719418 4720062) Hypothetical, unclassified, unknown 4724034 4722850 Transport of small molecules 4744136 4745123 DNA replication, recombination, modificat 4747136 4746639 Translation, post-translational modification 4754378 4753989 Translation, post-translational modification 4756472 4756083 Translation, post-translational modification 4756472 4756083 Translation, post-translational modification 4756472 4756083 Translation, post-translational modification 4756847 4756978 Protein secretion/export apparatus 4758451 4757123 Translation, post-translational modification 4758886 4758452 Translation, post-translational modification 4758986 4758465 Translation, post-translational modification 4759066 4758890 Translation, post-translational modification 4759066 4758890 Translation, post-translational modification 4759066 4758907 Translation, post-translational modification 4759069 4759093 Translation, post-translational modification 4759569 4759093 Translation, post-translational modification 4760467 4759934 Translation, post-translational modification 476047 4759934 Translation, post-translational modification 4760871 4760479 Translation, post-translational modification 4761919 4761380 Translation, post-translational modification 4762834 4762265 Translation, post-translational modification 4762834 4762265 Translation, post-translational modification 4763118 4762927 Translation, post-translational modification 476311 4763118 Translation, post-translational modification 4763531 4763118 Translation, post-translational modification 4763531 4763118 Translation, post-translational modification 4764862 4764587 Translation, post-translational modification 476477 477357 Translation, post-translational modification 4764862 4764587 Translation, post-translational modification 4764661 47648242 Translation, post-translational modification 476477 4772278 Translation, post-translational modification 4764862 4764587 Translation, post-translational modification 4764862 4764587 Translation, pos	Secreted Factors (toxins, enzymes, algina		
Transport of small molecules Transport of small molecules DNA replication, recombination, modificat Translation, post-translational modification Translation	Secreted Factors (toxins, enzymes, aigina		
Transport of small molecules DNA replication, recombination, modificat Translation, post-translational modification Translation, post-translational modific	Secreted Factors (toxins, enzymes, aigina		
Translation, post-translational modification Translation, post-tra	Hypothetical, unclassified, unknown		
Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Protein secretion/export apparatus Translation, post-translational modification Translation, post-translational	Transport of small molecules		
Transcription, RNA processing and degral Transcription, RNA processing and degral Translation, post-translational modification degral 4756466 4755446 4756466 Translation, post-translational modification degral 4756472 4756083 Translation, post-translational modification degral 4756472 4756083 Translation, post-translational modification degral 4756847 4756978 Protein secretion/export apparatus degral 4758451 4757123 Translation, post-translational modification degral 4758866 4758452 Translation, post-translational modification degral 4759066 4758890 Translation, post-translational modification degral 4759069 4760479 4760479 4760479 4760479 4760479 4760479 4760479 4761360 4761360 4761360 4761360 4761360 4761360 4761360 4761360 4762069 476206	DNA replication, recombination, modification		
Translation, post-translational modification Translation, post-tra	Translation, post-translational modification		
Translation, post-translational modification Translation, post-tra	Transcription, RNA processing and degra		
Translation, post-translational modification Translation, post-translational modification Protein secretion/export apparatus Protein secretion/export apparatus Translation, post-translational modification Translation, post-translational modificat	Translation, post-translational modification		
Translation, post-translational modification Protein secretion/export apparatus Translation, post-translational modification Translation, post-translational	Translation, post-translational modification		
Protein secretion/export apparatus Translation, post-translational modification Translation, post-translational	Translation, post-translational modification		
Translation, post-translational modification Translation, post-tra	Translation, post-translational modification		
Translation, post-translational modification Translation, post-tra	Protein secretion/export apparatus		
Translation, post-translational modification Translation, post-tra	Translation, post-translational modification		
Translation, post-translational modification Translation, post-tra	Translation, post-translational modification		
Translation, post-translational modification Transcription, RNA processing and degra Transcription, RNA processing and degra Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational	Translation, post-translational modification		
Translation, post-translational modification Transcription, RNA processing and degre Transcription, RNA processing and degre Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational	Translation, post-translational modification		
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Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Transcription, RNA processing and degra Translation, post-translational modification Translation, post-translat	Translation, post-translational modification		4763118
Translation, post-translational modification 4764574 4764587 Translation, post-translational modification 4765700 4764879 Translation, post-translational modification 4765700 4764879 Translation, post-translational modification 4766011 4765712 Translation, post-translational modification 4766610 4766008 Translation, post-translational modification 4767259 4766624 Translation, post-translational modification 4767653 4767342 Translation, post-translational modification 4771655 4771185 Translation, post-translational modification 4772126 4771755 Transcription, RNA processing and degra 4780616 4776543 Translation, post-translational modification 4781206 4780838 Translation, post-translational modification 4781785 4781285 Translation, post-translational modification 4782679 4781984 Translation, post-translational modification 4783110 4782679 Transcription, RNA processing and degra 4783760 4783227 Protein secretion/export apparatus 4784138 4783770 Hypothetical, unclassified, unknown 4819927 4820409 Two-component regulatory systems 4820531 4821358 Hypothetical, unclassified, unknown 4823363 4823079 Hypothetical, unclassified, unknown 4823363 4823079 Hypothetical, unclassified, unknown 4823363 4823079	Translation, post-translational modification		4763543
Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Transcription, RNA processing and degra Transcription, RNA processing and degra Translation, post-translational modification Translation, post-translational	Translation, post-translational modification	4764574	4764242
Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Transcription, RNA processing and degra Translation, post-translational modification Translation, post-translat	Translation, post-translational modification	4764862	4764587
Translation, post-translational modification 476610 476608 Translation, post-translational modification 4767259 476624 Translation, post-translational modification 4767259 476624 Translation, post-translational modification 4767653 4767342 Translation, post-translational modification 4771655 4771185 Translation, post-translational modification 4772126 4771755 Transcription, RNA processing and degra 4780616 4776543 Translation, post-translational modification 4781206 4780838 Translation, post-translational modification 4781785 4781285 Translation, post-translational modification 4782679 4781984 Translation, post-translational modification 4783110 4782679 Transcription, RNA processing and degra 4783760 4783227 Protein secretion/export apparatus 4784138 4783770 Hypothetical, unclassified, unknown 4819927 4820409 Two-component regulatory systems 4820531 4821358 Hypothetical, unclassified, unknown 4823363 4823079 Hypothetical, unclassified, unknown 4824123 4823386	Translation, post-translational modification	4765700	
Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Transcription, RNA processing and degral Transcription, RNA processing and degral Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Transcription, RNA processing and degral Transcription, RNA processing	Translation, post-translational modification	4766011	
Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Transcription, RNA processing and degra Transcription, RNA processing and degra Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Transcription, RNA processing and degra Transcription, 4781206 Transcrip	Translation, post-translational modification	4766610	
Translation, post-translational modification 4767653 4767342 Translation, post-translational modification 4771655 4771185 Translation, post-translational modification 4772126 4771755 Transcription, RNA processing and degra 4780616 4776543 Translation, post-translational modification 4781206 4780838 Translation, post-translational modification 4781785 4781285 Translation, post-translational modification 4782679 4781984 Translation, post-translational modification 4783110 4782679 Transcription, RNA processing and degra 4783760 4783227 Protein secretion/export apparatus 4784138 4783770 Hypothetical, unclassified, unknown 4819927 4820409 Two-component regulatory systems 4820531 4823368 Hypothetical, unclassified, unknown 4823363 4823079 Hypothetical, unclassified, unknown 4824123 4823386	Translation, post-translational modification	4767259	
Translation, post-translational modification Translation, post-translational modification Transcription, RNA processing and degrar Transcription, RNA processing and degrar Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Transcription, RNA processing and degrar Transcription, RNA processing and degr	Translation, post-translational modification	4767653	
Translation, post-translational modification Transcription, RNA processing and degra Transcription, RNA processing and degra Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Translation, post-translational modification Transcription, RNA processing and degra Transc	Translation, post-translational modification	4771655	
Transcription, RNA processing and degra 4776477 4772276 Transcription, RNA processing and degra 4780616 4776543 Translation, post-translational modification 4781206 4780838 Translation, post-translational modification 4781785 4781285 Translation, post-translational modification 4782679 4781984 Translation, post-translational modification 4783110 4782679 Transcription, RNA processing and degra 4783760 4783227 Protein secretion/export apparatus 4784138 4783770 Hypothetical, unclassified, unknown 4819927 4820409 Two-component regulatory systems 4820531 4821358 Hypothetical, unclassified, unknown 4823363 4823079 Hypothetical, unclassified, unknown 4824123 4823386	Translation, post-translational modification	4772126	
Transcription, RNA processing and degral 4780616 4776543 Translation, post-translational modification 4781206 4780838 Translation, post-translational modification 4781785 4781285 Translation, post-translational modification 4782679 4781984 Translation, post-translational modification 4783110 4782679 Transcription, RNA processing and degral 4783760 4783227 Protein secretion/export apparatus 4784138 4783770 Hypothetical, unclassified, unknown 4787479 4786733 Hypothetical, unclassified, unknown 4819927 4820409 Two-component regulatory systems 4820531 4821358 Hypothetical, unclassified, unknown 4823363 4823079 Hypothetical, unclassified, unknown 4824123 4823386	Transcription, RNA processing and degra	4//04//	
Translation, post-translational modification 4781206 4780838 Translation, post-translational modification 4781785 4781285 Translation, post-translational modification 4782679 4781984 Translation, post-translational modification 4783110 4782679 Transcription, RNA processing and degra 4783760 4783227 Protein secretion/export apparatus 4784138 4783770 Hypothetical, unclassified, unknown 4787479 4786733 Hypothetical, unclassified, unknown 4819927 4820409 Two-component regulatory systems 4820531 4821358 Hypothetical, unclassified, unknown 4823363 4823079 Hypothetical, unclassified, unknown 4824123 4823386	Transcription, RNA processing and degra		
Translation, post-translational modification 4781785 4781285 Translation, post-translational modification 4782679 4781984 Translation, post-translational modification 4783110 4782679 Transcription, RNA processing and degra 4783760 4783227 Protein secretion/export apparatus 4784138 4783770 Hypothetical, unclassified, unknown 4787479 4786733 Hypothetical, unclassified, unknown 4819927 4820409 Two-component regulatory systems 4820531 4821358 Hypothetical, unclassified, unknown 4823363 4823079 Hypothetical, unclassified, unknown 4824123 4823386	Translation, post-translational modification		
Translation, post-translational modification 4782679 4781984 Translation, post-translational modification 4783110 4782679 Transcription, RNA processing and degra 4783760 4783227 Protein secretion/export apparatus 4784138 4783770 Hypothetical, unclassified, unknown 4787479 4786733 Hypothetical, unclassified, unknown 4819927 4820409 Two-component regulatory systems 4820531 4821358 Hypothetical, unclassified, unknown 4823363 4823079 Hypothetical, unclassified, unknown 4824123 4823386	Translation, post-translational modification	4781785	
Translation, post-translational modification 4783110 4782679 Transcription, RNA processing and degra 4783760 4783227 Protein secretion/export apparatus 4784138 4783770 Hypothetical, unclassified, unknown 4787479 4786733 Hypothetical, unclassified, unknown 4819927 4820409 Two-component regulatory systems 4820531 4821358 Hypothetical, unclassified, unknown 4823363 4823079 Hypothetical, unclassified, unknown 4824123 4823386	Translation, post-translational modification	1 4782679	
Transcription, RNA processing and degra 4783760 4783227 Protein secretion/export apparatus 4784138 4783770 Hypothetical, unclassified, unknown 4787479 4786733 Hypothetical, unclassified, unknown 4819927 4820409 Two-component regulatory systems 4820531 4821358 Hypothetical, unclassified, unknown 4823363 4823079 Hypothetical, unclassified, unknown 4824123 4823386	Translation, post-translational modification	1 4783110	
Protein secretion/export apparatus 4784138 4783770 Hypothetical, unclassified, unknown 4787479 4786733 Hypothetical, unclassified, unknown 4819927 4820409 Two-component regulatory systems 4820531 4821358 Hypothetical, unclassified, unknown 4823363 4823079 Hypothetical, unclassified, unknown 4824123 4823386	Transcription, RNA processing and degra	4783760	
Hypothetical, unclassified, unknown Two-component regulatory systems Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown	Protein secretion/export apparatus		
Hypothetical, unclassified, unknown Two-component regulatory systems Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown	Hypothetical, unclassified, unknown		
Two-component regulatory systems 4820531 4821358 Hypothetical, unclassified, unknown 4823363 4823079 Hypothetical, unclassified, unknown 4824123 4823386	Hypothetical, unclassified, unknown		
Hypothetical, unclassified, unknown 4823363 4823079 Hypothetical, unclassified, unknown 4824123 4823386	Two-component regulatory systems		
Involutetical, dilotacomos, sincitori	Hypothetical, unclassified, unknown		
Hypothetical, unclassified, unknown 4830553 4829642	Hypothetical, unclassified, unknown		
	Hypothetical, unclassified, unknown	4830553	4629042

	4920063	4831181
Hypothetical, unclassified, unknown	4830963	4842700
Nucleotide biosynthesis and metabolism	4843551	4852316
Hypothetical, unclassified, unknown	4851309	4853649
Hypothetical, unclassified, unknown	4854008	
Carbon compound catabolism	4856959	4858410 4858489
Putative enzymes	4859262	
Transcriptional regulators	4870327	4869557
Hypothetical, unclassified, unknown	4875244	4874654
Hypothetical, unclassified, unknown	4877605	4876820
Hypothetical, unclassified, unknown	4878586	4877690
Hypothetical, unclassified, unknown	4878789	4879544
Hypothetical, unclassified, unknown	4882052	4882354
Hypothetical, unclassified, unknown	4884960	4884718
Hypothetical, unclassified, unknown	4887505	4887278
Adaptation, protection	4893696	4894277
Hypothetical, unclassified, unknown	4902201	4903295
Hypothetical, unclassified, unknown	4909403	4909161
Hypothetical, unclassified, unknown	4914509	4914126
Chaperones & heat shock proteins	4917123	4915480
Chaperones & heat shock proteins	4917467	4917174
Hypothetical, unclassified, unknown	4918932	4918198
Putative enzymes	4919041	4919799
Hypothetical, unclassified, unknown	4921980	4922363
Hypothetical, unclassified, unknown	4925794	4925315
Protein secretion/export apparatus	4936615	4933865
Hypothetical, unclassified, unknown	4937819	4938214
Cell wall / LPS / capsule	4939186	4938275
Cell division	4940483	4939299
Cell division	4941787	4940534
Cell division	4942672	4941809
Cell wall / LPS / capsule	4945074	4943632
Cell wall / LPS / capsule	4946140	4945067
Cell division	4947329	4946130
Cell wall / LPS / capsule	4948675	4947329
Cell wall / LPS / capsule	4949771	4948689
Cell wall / LPS / capsule	4951147	4949771
Cell wall / LPS / capsule	4952603	4951140
Cell wall / LPS / capsule	4954342	4952603
Cell division	4954632	4954339
Hypothetical, unclassified, unknown	4955570	4954629
Hypothetical, unclassified, unknown	4956028	4955573
Hypothetical, unclassified, unknown	4959519	4959896
Putative enzymes	4959925	4960518
Adaptation, protection	4961557	4961150
Adaptation, protection	4962186	
Energy metabolism	4964265	
Translation, post-translational modification		
Translation, post-translational modification	on 4965943	
Translation, post-translational modification	4968711	
Hypothetical, unclassified, unknown	4971890	
Translation, post-translational modification		
Hansiation, post-translational mounication	4974028	
Hypothetical, unclassified, unknown	1 4874020	7070000

Cell wall / LPS / capsule	4985469	4984204
Hypothetical, unclassified, unknown	4986154	4985846
Hypothetical, unclassified, unknown	4986798	4986151
Hypothetical, unclassified, unknown	4987283	4986810
Transport of small molecules	4988081	4987284
Hypothetical, unclassified, unknown	4989304	4990284
Hypothetical, unclassified, unknown	4990832	4991404
Hypothetical, unclassified, unknown	4991391	4991918
Transport of small molecules	4991918	4992643
Transcriptional regulators	4992869	4994362
Hypothetical, unclassified, unknown	4994440	4994748
Transport of small molecules	4994762	4995226
Transport of small molecules	4996118	4996390
Hypothetical, unclassified, unknown	5000303	4999908
Cell division	5012313	5011321
Cell division	5013430	5012393
Translation, post-translational modificatio		5013960
Translation, post-translational modificatio		5015427
Translation, post-translational modificatio		5016979
Hypothetical, unclassified, unknown	5017039	5017416
Hypothetical, unclassified, unknown	5028230	5027421
Transcriptional regulators	5036244	5036807
Hypothetical, unclassified, unknown	5046663	5046031
Biosynthesis of cofactors, prosthetic grou	5068031	5068879
Motility & Attachment	5069530	5069081
Motility & Attachment	5069762	5071462
Motility & Attachment	5071566	5072690
Hypothetical, unclassified, unknown	5073563	5074174
Hypothetical, unclassified, unknown	5074171	5074371
Hypothetical, unclassified, unknown	5077535	5077705
Transcription, RNA processing and degra	5091814	5090852
Two-component regulatory systems	5094984	5096321
Motility & Attachment	5099262	5100086
Motility & Attachment	5100083	5100670
Adaptation, protection	5105929	
Translation, post-translational modification	5106957	
Translation, post-translational modification	oh 5109781	
Biosynthesis of cofactors, prosthetic grou	5110743	
Translation, post-translational modification	oh 5112662	
Hypothetical, unclassified, unknown	5113468	
Amino acid biosynthesis and metabolism	5114598	
Adaptation, protection	5115889	
Translation, post-translational modification	on 5116288	
Translation, post-translational modification	oh 5116623	
Biosynthesis of cofactors, prosthetic gro	u 5116864	
Hypothetical, unclassified, unknown	5122386	
Hypothetical, unclassified, unknown	512290	
Hypothetical, unclassified, unknown	5125930	
Hypothetical, unclassified, unknown	513581	
Transcriptional regulators	5155560	
Hypothetical, unclassified, unknown	5162448	
Hypothetical, unclassified, unknown	516875	516918

		5400050
Hypothetical, unclassified, unknown	5169504	5169250
Hypothetical, unclassified, unknown	5174979	5176103
Hypothetical, unclassified, unknown	5197880	5198323
Hypothetical, unclassified, unknown	5204927	5206087
Hypothetical, unclassified, unknown	5206486	5206208
Hypothetical, unclassified, unknown	5207006	5206719
Hypothetical, unclassified, unknown	5210995	5210705
Hypothetical, unclassified, unknown	5212104	5211631
Nucleotide biosynthesis and metabolism	5212832	5213470
Hypothetical, unclassified, unknown	5215669	5216202
Chaperones & heat shock proteins	5216763	5217551
Biosynthesis of cofactors, prosthetic grou	5223561	5222539
Cell wall / LPS / capsule	5230910	5230113
Biosynthesis of cofactors, prosthetic grou	5231658	5230900
Translation, post-translational modification		5232484
Translation, post-translational modification		5233584
Cell wall / LPS / capsule	5236773	5237390
Biosynthesis of cofactors, prosthetic grou	5237392	5238240
Nucleotide biosynthesis and metabolism	5238407	5239348
Translation, post-translational modification		5240079
Translation, post-translational modification		5240705
Translation, post-translational mountcation	5242558	5242253
Hypothetical, unclassified, unknown	5246122	5245475
Putative enzymes	5248771	5248070
Hypothetical, unclassified, unknown	5250617	5249598
Hypothetical, unclassified, unknown	5272299	5271484
Fatty acid and phospholipid metabolism	5275731	5274007
Amino acid biosynthesis and metabolism	5276282	5276734
Hypothetical, unclassified, unknown	5277171	5276842
Hypothetical, unclassified, unknown	5277950	5277171
Hypothetical, unclassified, unknown	5282158	5282505
Hypothetical, unclassified, unknown	5286034	5285267
Transport of small molecules	5291613	5291960
Hypothetical, unclassified, unknown	5297482	5297006
Hypothetical, unclassified, unknown		5311213
Biosynthesis of cofactors, prosthetic group		5312263
Biosynthesis of cofactors, prosthetic group		5313585
Biosynthesis of cofactors, prosthetic grou	5313675	
Energy metabolism	5322234	
Hypothetical, unclassified, unknown	5322706	
Hypothetical, unclassified, unknown	5323100	
Hypothetical, unclassified, unknown		
Transcription, RNA processing and degra		
Translation, post-translational modification	5325921	
Translation, post-translational modification	5329948	
Transcription, RNA processing and degra	5331457	
Hypothetical, unclassified, unknown	5331960	
Protein secretion/export apparatus	5332742	
Energy metabolism	5333500	
Cell wall / LPS / capsule	5334903	
Biosynthesis of cofactors, prosthetic grou	5335771	
Cell division	5338522	
Hypothetical, unclassified, unknown	5338617	5338931

	5343754	53431041
Hypothetical, unclassified, unknown	5345891	5345085
Amino acid biosynthesis and metabolism	5349760	5349200
Chaperones & heat shock proteins	5352078	5351674
Transcriptional regulators	5352076	5352706
Transport of small molecules	5353506	5353072
Hypothetical, unclassified, unknown	5361585	5362067
Hypothetical, unclassified, unknown	5364070	5364735
Two-component regulatory systems		5366654
Transcriptional regulators	5366256 5370720	5370475
Hypothetical, unclassified, unknown	5376720	5377708
Hypothetical, unclassified, unknown	5377790	5378095
Hypothetical, unclassified, unknown	5378092	5378841
Hypothetical, unclassified, unknown	5378092	5379512
Hypothetical, unclassified, unknown		5382795
Related to phage, transposon, or plasmid	5383811	5387721
Hypothetical, unclassified, unknown	5386999 5396858	5395929
Energy metabolism	5402944	5402015
Fatty acid and phospholipid metabolism		5414278
Hypothetical, unclassified, unknown	5414487	5418350
Hypothetical, unclassified, unknown	5418568	5420317
Hypothetical, unclassified, unknown	-5419862	5423065
Transcriptional regulators	5422505 5434651	5434115
Hypothetical, unclassified, unknown	5442303	5442773
Fatty acid and phospholipid metabolism	5442303	5444140
Fathy acid and phospholipid metabolisii		5446082
Translation, post-translational modificatio	5448642	5448965
Transcription, RNA processing and degra	5460525	5461382
Transport of small molecules	5462762	5463604
Central intermediary metabolism	5463917	5464435
Hypothetical, unclassified, unknown	5464820	5466520
Central intermediary metabolism	5468282	5468016
Hypothetical, unclassified, unknown	5468408	5469022
Hypothetical, unclassified, unknown	5472041	5471625
Hypothetical, unclassified, unknown	5472438	5472734
Hypothetical, unclassified, unknown	5473765	5474577
Transcriptional regulators	5480401	5481090
Two-component regulatory systems	5483767	
Transport of small molecules	5486355	
Hypothetical, unclassified, unknown Biosynthesis of cofactors, prosthetic gro		
Biosynthesis of colactors, prostrictio gro	5489040	
Hypothetical, unclassified, unknown	5490651	
Transcriptional regulators	5505783	
Transcriptional regulators Hypothetical, unclassified, unknown	5507897	5506965
Hypothetical, unclassified, unknown	5517093	5516398
Hypothetical, unclassified, unknown		
Biosynthesis of cofactors, prosthetic gro Hypothetical, unclassified, unknown	552238	
Hypothetical, unclassified, unknown	5524718	
Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown	5525904	
DNA replication, recombination, modific		
Translation, post-translational modificat		
Translation, post-translational modificat		
Translation, post-translational modificat		

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Nucleotide biosynthesis and metabolism	5543364	5542072
Hypothetical, unclassified, unknown	5544820	5544635
Hypothetical, unclassified, unknown	5548644	5548396
Translation, post-translational modification	5549721	5548750
Hypothetical, unclassified, unknown	5553583	5553116
Hypothetical, unclassified, unknown	5556934	5557953
Central intermediary metabolism	5561598	5562413
Hypothetical, unclassified, unknown	5569089	5570627
Hypothetical, unclassified, unknown	5570624	5571160
DNA replication, recombination, modificat	5574485	5572221
Hypothetical, unclassified, unknown	5575017	5574493
Hypothetical, unclassified, unknown	5576027	5575014
DNA replication, recombination, modificat	5577916	5576027
Hypothetical, unclassified, unknown	5579498	5578680
Hypothetical, unclassified, unknown	5580961	5581707
Putative enzymes	5593423	5592632
Cell wall / LPS / capsule	5605097	5603820
Antibiotic resistance and susceptibility	5606102	5606434
Hypothetical, unclassified, unknown	5606495	5607670
Hypothetical, unclassified, unknown	5607667	5608479
Transport of small molecules	5615543	5613732
Transport of small molecules	5615651	5616301
Hypothetical, unclassified, unknown	5626378	5624900
Hypothetical, unclassified, unknown	5627133	5626375
Hypothetical, unclassified, unknown	5627864	5627130
Hypothetical, unclassified, unknown	5628670	5627864
Cell wall / LPS / capsule	5629788	5628667
Cell wall / LPS / capsule	5630852	5629785
Cell wall / LPS / capsule	5631886	5630849
Cell wall / LPS / capsule	5659184	5658417
Hypothetical, unclassified, unknown	5662741	5663814
Transcriptional regulators Hypothetical, unclassified, unknown	5663888	5664868
Hypothetical, unclassified, unknown		5664989
Biosynthesis of cofactors, prosthetic grou	5675701	5675183
Amino acid biosynthesis and metabolism	5680712	5679648
Motility & Attachment		5689714
DNA replication, recombination, modification		5691726
Translation, post-translational modification	5691761	5692456
Hypothetical, unclassified, unknown	5702113	5701697
Hypothetical, unclassified, unknown		
Biosynthesis of cofactors, prosthetic group	5703453	
Hypothetical, unclassified, unknown	5704076	
Hypothetical, unclassified, unknown		
Amino acid biosynthesis and metabolism	5706551	5706799
Protein secretion/export apparatus		
Hypothetical, unclassified, unknown	5708035	
Chemotaxis	5708954	
Hypothetical, unclassified, unknown	5720468	
Transcriptional regulators	5723581	
Carbon compound catabolism	5753473	
Central intermediary metabolism	5754143	
Transcriptional regulators	5762149	
Amino acid biosynthesis and metabolism	5766483	5767892

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Protein secretion/export apparatus 5777096 5776957 5777133 Nucleotide biosynthesis and metabolism 5777887 5777389 5777389 5777389 5777389 5777389 5777389 5777808 5777989 5777889 5777389 5777880 5777880 5777880 5777880 5777880 5777880 5779880 5779044 4			577000E
Hypothetical, unclassified, unknown	Protein secretion/export apparatus	5777096	5776605
Appointment Appointment	Nucleotide biosynthesis and metabolism		
Amino acid biosynthesis and metabolism 5791985 5790444	Hypothetical, unclassified, unknown		
Hypothetical, unclassified, unknown	Carbon compound catabolism		
Amino acid biosynthesis and metabolism 5791885 5792234 Hypothetical, unclassified, unknown 5791836 5792234 Hypothetical, unclassified, unknown 5797064 5797336 Transport of small molecules 5802128 5802823 Cell wall / LPS / capsule 5811335 5812240 Cell wall / LPS / capsule 5812240 5813121 Cell wall / LPS / capsule 5813121 5813661 Amino acid biosynthesis and metabolism 5824786 5825718 Hypothetical, unclassified, unknown 5839499 5828903 Hypothetical, unclassified, unknown 5835481 5835791 Hypothetical, unclassified, unknown 5835481 5835894 Putative enzymes 5840894 5839194 Putative enzymes 5843799 5843797 Hypothetical, unclassified, unknown 5883012 5881979 Translation, post-translational modification 5883012 5881678 Hypothetical, unclassified, unknown 5883971 5884285 Hypothetical, unclassified, unknown 5883972 5895260 Hypotheti	Hypothetical, unclassified, unknown		
Hypothetical, unclassified, unknown	Amino acid biosynthesis and metabolism		
Hypothetical, unclassified, unknown	Hypothetical, unclassified, unknown		
Transport of small molecules 5802128 5802823 Cell wall / LPS / capsule 5810380 58113335 5812243 Cell wall / LPS / capsule 5813121 5813121 5813121 Cell wall / LPS / capsule 5813121 5813666 Amino acid biosynthesis and metabolism 5824786 5825718 Hypothetical, unclassified, unknown 5830749 5830312 Hypothetical, unclassified, unknown 5836481 5835894 Hypothetical, unclassified, unknown 5836481 5835894 Hypothetical, unclassified, unknown 5840894 5839104 Putative enzymes 5840894 5839104 Chaperones & heat shock proteins 5840886 5847971 Putative enzymes 5879970 5878753 Hypothetical, unclassified, unknown 5883481 5889999 Translation, post-translational modification 5883012 5881678 Hypothetical, unclassified, unknown 5883971 5884285 Hypothetical, unclassified, unknown 5885485 5885943 Hypothetical, unclassified, unknown 5907389 5907862<	Hypothetical, unclassified, unknown		
Cell wall / LPS / capsule 5810280 5811335 5812243 5812243 5813221 5813121 5813121 5813121 5813121 58131221 58131221 5813666 5813121 5813666 5813121 5813666 5813121 5813666 5813121 5813666 5813121 5813666 5813121 5813666 5825718 581966 5824786 5825718 5826718 5826718 5826718 5826718 5828903 149000 5828903 149000 5828903 149000 5830749 5830312 584830312 5848361 58393104 149000 149000 5835894 5835894 149000 149000 5843366 5847971 58483197 5848366 5847971 5879790 5878753 149000 5879790 5878753 149000 149000 5883612 5881678 149000 149000 5883612 5881678 149000 149000 5883661 5883921 5881678 149000 149000 5883561 5883202 149000 149000 <t< td=""><td>Transport of small molecules</td><td>5802128</td><td></td></t<>	Transport of small molecules	5802128	
Cell wall / LPS / capsule 5811335 5812243 Cell wall / LPS / capsule 5813121 5813121 Cell wall / LPS / capsule 5813121 5813121 Amino acid biosynthesis and metabolism 5824786 5825718 Hypothetical, unclassified, unknown 5829469 5828903 Hypothetical, unclassified, unknown 5830749 5830312 Hypothetical, unclassified, unknown 5840894 5839104 Putative enzymes 5840894 5839104 Putative enzymes 5843799 5843197 Chaperones & heat shock proteins 5848366 5847971 Putative enzymes 587970 5878753 Hypothetical, unclassified, unknown 5880412 5880712 Translation, post-translational modification 5883012 5881678 Hypothetical, unclassified, unknown 5883576 5883022 Hypothetical, unclassified, unknown 5885485 5885485 Hypothetical, unclassified, unknown 5896726 5895260 Transcription, RNA processing and degre 5900123 5898644 Energy metabolism	Cell wall / LPS / capsule	5810280	
Cell wall / LPS / capsule 5812240 5813121 5813666 Amino acid biosynthesis and metabolism 5824786 5825718 Hypothetical, unclassified, unknown 5829469 5828903 Hypothetical, unclassified, unknown 5830749 5830312 Hypothetical, unclassified, unknown 5835481 5835894 Putative enzymes 5840894 5839104 Putative enzymes 5843799 5843197 Chaperones & heat shock proteins 5848366 5847971 Putative enzymes 5879970 5878753 Hypothetical, unclassified, unknown 5880481 5879999 Translation, post-translational modification 5883012 5881678 Hypothetical, unclassified, unknown 5883971 5884285 Hypothetical, unclassified, unknown 5885485 58859260 Transcription, RNA processing and degra 5900123 589864 Energy metabolism 5907389 5907862 Hypothetical, unclassified, unknown 590329 5907847 Biosynthesis of cofactors, prosthetic grou 5922449 5920741	Cell wall / LPS / capsule	5811335	
Cell wall / LPS / capsule 5813121 5813665 Amino acid biosynthesis and metabolism 5824786 5825718 Hypothetical, unclassified, unknown 5829469 5828903 Hypothetical, unclassified, unknown 5830749 5830312 Hypothetical, unclassified, unknown 5835481 5835894 Putative enzymes 5840894 5839104 Putative enzymes 5843799 5843197 Chaperones & heat shock proteins 5848366 5847971 Putative enzymes 5679970 5878753 Hypothetical, unclassified, unknown 5880481 5879999 Translation, post-translational modification 5883012 5881678 Hypothetical, unclassified, unknown 5883971 5884285 Hypothetical, unclassified, unknown 5885485 5885943 Hypothetical, unclassified, unknown 5896726 5895260 Transcription, RNA processing and degra 5900123 5898864 Energy metabolism 5907389 5907862 Hypothetical, unclassified, unknown 5908329 5907847 Biosynthesis of cofac		5812240	
Amino acid biosynthesis and metabolism 582/4786 582/578 Hypothetical, unclassified, unknown 5830749 5829893 Hypothetical, unclassified, unknown 5835481 5835894 Hypothetical, unclassified, unknown 5835481 5835894 Putative enzymes 5840894 5839104 Putative enzymes 5843799 5843197 Chaperones & heat shock proteins 5848366 5847971 Putative enzymes 5879970 5878753 Hypothetical, unclassified, unknown 5880481 5879999 Translation, post-translational modification 5883012 5881678 Hypothetical, unclassified, unknown 5883576 5883022 Hypothetical, unclassified, unknown 5885485 5885943 Hypothetical, unclassified, unknown 5896726 5895260 Transcription, RNA processing and degra 5900123 5898864 Energy metabolism 5900694 5900368 Hypothetical, unclassified, unknown 5907389 5907622 Hypothetical, unclassified, unknown 5908329 5907847 Biosynthes	Cell wall / LPS / capsule		
Hypothetical, unclassified, unknown 5829469 5828903 Hypothetical, unclassified, unknown 5830749 5830312 Hypothetical, unclassified, unknown 5836841 5835894 Putative enzymes 5840894 5839104 Putative enzymes 5843799 5843197 Chaperones & heat shock proteins 5848366 5847971 Putative enzymes 5879970 5878753 Hypothetical, unclassified, unknown 5880481 5879999 Translation, post-translational modification 5883012 5881678 Hypothetical, unclassified, unknown 5883971 5884285 Hypothetical, unclassified, unknown 5885485 5885943 Hypothetical, unclassified, unknown 5895260 5900694 5900368 Transcription, RNA processing and degral 5900694 5900368 Hypothetical, unclassified, unknown 5907389 5907862 Hypothetical, unclassified, unknown 5908329 5907847 Biosynthesis of cofactors, prosthetic grou 5921496 5920741 Biosynthesis of cofactors, prosthetic grou 5941081	Amino acid biosynthesis and metabolism	5824786	5825718
Hypothetical, unclassified, unknown Hypothetical, unclassified, un	Hypothetical unclassified unknown	5829469	
Hypothetical, unclassified, unknown 5835481 5835894 Putative enzymes 5840894 5839104 Putative enzymes 5843799 5843197 Chaperones & heat shock proteins 5848366 5847971 Putative enzymes 5879970 5878753 Hypothetical, unclassified, unknown 5880481 5879999 Hypothetical, unclassified, unknown 5883576 5883022 Hypothetical, unclassified, unknown 5883971 5884285 Hypothetical, unclassified, unknown 5885485 5885943 Hypothetical, unclassified, unknown 5896726 5895260 Hypothetical, unclassified, unknown 5900123 5898864 Energy metabolism 5900694 5900368 Hypothetical, unclassified, unknown 5907389 5907862 Hypothetical, unclassified, unknown 590329 5907847 Biosynthesis of cofactors, prosthetic grou 5921496 5920741 Biosynthesis of cofactors, prosthetic grou 5922434 5921493 Hypothetical, unclassified, unknown 5941081 5940746 Cell wall / LPS / capsule 5941335 5941475 Amino acid biosynthesis and metabolism 5942744 5943574 Putative enzymes 5945234 5945932 Central intermediary metabolism 5952820 5952482 DNA replication, recombination, modificat 5969764 5969784 Energy metabolism 5969764 5969784 DNA replication, recombination, modificat 5989319 598645 DNA replication, recombination, modificat 5989319 5988645 DNA replication, recombination, modificat 5989319 5989667 Nucleotide biosynthesis and metabolism 5990675 5991130 Hypothetical, unclassified, unknown 5990035 5999065 Energy metabolism 6000142 5999753 Hypothetical, unclassified, unknown 6003329 6002958 Hypothetical, unclassified, unknown 600329 6002958 Transcription, RNA processing and degra 6004095 6003376	Hypothetical unclassified unknown	5830749	
Putative enzymes	Hypothetical unclassified unknown		5835894
Putative enzymes 5843799 5843197 Putative enzymes 5848366 5847971 Putative enzymes 5879970 5878753 Pypothetical, unclassified, unknown 5880481 5879990 Translation, post-translational modification 5883012 5881678 Hypothetical, unclassified, unknown 5883576 5883022 Hypothetical, unclassified, unknown 5883971 5884285 Hypothetical, unclassified, unknown 5885485 5885943 Hypothetical, unclassified, unknown 5896726 5895260 Transcription, RNA processing and degra 5900123 5898864 Energy metabolism 5900694 5900368 Hypothetical, unclassified, unknown 5907389 5907867 Hypothetical, unclassified, unknown 5908329 5907847 Biosynthesis of cofactors, prosthetic grou 5921496 5920741 Biosynthesis of cofactors, prosthetic grou 5922434 5921493 Hypothetical, unclassified, unknown 5941081 5940746 Cell wall / LPS / capsule 5941335 5941475 Amino acid biosynthesis and metabolism 5942744 5943574 Putative enzymes 5945234 5945932 Central intermediary metabolism 5962715 5964724 Energy metabolism 5969764 5969354 Hypothetical, unclassified, unknown 5972202 5971849 DNA replication, recombination, modificat 5989459 5990667 Nucleotide biosynthesis and metabolism 5990675 5991130 Hypothetical, unclassified, unknown 5990675 5991130 Hypothetical, unclassified, unknown 6001377 6000760 Nucleotide biosynthesis and metabolism 6002039 6001398 Hypothetical, unclassified, unknown 6003329 6002958 Transcription, RNA processing and degra 6004095 6003376			5839104
Chaperones & heat shock proteins Putative enzymes S879970 S878753 Hypothetical, unclassified, unknown Translation, post-translational modification Hypothetical, unclassified, unknown Hypothetical, unclassified,		5843799	5843197
Putative enzymes Hypothetical, unclassified, unknown Fypothetical, unclassified, unknown Fypothetical, unclassified, unknown Hypothetical,	Changrongs & heat shock proteins		5847971
Hypothetical, unclassified, unknown Translation, post-translational modification Hypothetical, unclassified, unknown Hypothetical, unclass			5878753
Translation, post-translational modification 5883012 5881076 5883022 Hypothetical, unclassified, unknown 5883576 5883022 Hypothetical, unclassified, unknown 5883971 5884285 Hypothetical, unclassified, unknown 5885485 5885943 Hypothetical, unclassified, unknown 5896726 5895260 Transcription, RNA processing and degra 5900123 5898864 Energy metabolism 5900694 5900368 Hypothetical, unclassified, unknown 5907389 5907862 Hypothetical, unclassified, unknown 5908329 5907847 Biosynthesis of cofactors, prosthetic grou 5921496 5920741 Biosynthesis of cofactors, prosthetic grou 5922434 5921493 Hypothetical, unclassified, unknown 5941081 5940746 Cell wall / LPS / capsule 5941335 5941475 Amino acid biosynthesis and metabolism 5942744 5943574 Putative enzymes 5945234 5945932 Central intermediary metabolism 5952820 5952482 DNA replication, recombination, modifical 5962715 5964724 Energy metabolism 5972202 5971849 Translation, post-translational modification 5986118 5985882 DNA replication, recombination, modifical 598919 598645 DNA replication, recombination, modifical 598919 598685 DNA replication, recombination, modifical 598919 598685 DNA replication, recombination, modifical 598919 598667 Nucleotide biosynthesis and metabolism 5990675 5991130 Hypothetical, unclassified, unknown 5996035 5996985 Energy metabolism 6000142 5999753 Hypothetical, unclassified, unknown 6001377 6000760 Nucleotide biosynthesis and metabolism 6002039 6001398 Hypothetical, unclassified, unknown 600329 6002958 Transcription, RNA processing and degra 6004095 6003376	Unathetical unclassified unknown		5879999
Hypothetical, unclassified, unknown Hypothetical, unclassified, un	Translation post translational modification		5881678
Hypothetical, unclassified, unknown Hypothetical, unclassified, un	Hypothetical unclassified unknown	5883576	5883022
Hypothetical, unclassified, unknown Hypothetical, unclassified, un	Hypothetical unclassified unknown		
Hypothetical, unclassified, unknown Transcription, RNA processing and degra Energy metabolism Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown Biosynthesis of cofactors, prosthetic grou Biosynthesis of cofactors, prosthetic grou Biosynthesis of cofactors, prosthetic grou Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown Cell wall / LPS / capsule Amino acid biosynthesis and metabolism Putative enzymes Central intermediary metabolism DNA replication, recombination, modificat Energy metabolism Hypothetical, unclassified, unknown Franslation, post-translational modification DNA replication, recombination, modificat DNA replication, re	Hypothetical unclassified unknown		5885943
Transcription, RNA processing and degra 5900123 5898864 Energy metabolism 5900694 5900368 Hypothetical, unclassified, unknown 5907389 5907862 Hypothetical, unclassified, unknown 5908329 5907847 Biosynthesis of cofactors, prosthetic grou 5921496 5920741 Biosynthesis of cofactors, prosthetic grou 592434 5921493 Hypothetical, unclassified, unknown 5941081 5940746 Cell wall / LPS / capsule 5941335 5941475 Amino acid biosynthesis and metabolism 5942744 5943674 Putative enzymes 5945234 5952482 DNA replication, recombination, modificat 5962715 5964724 Energy metabolism 5969764 5969354 Hypothetical, unclassified, unknown 5972202 5971849 Translation, post-translational modification 5986118 5985882 DNA replication, recombination, modificat 5989319 5988645 DNA replication, recombination, modificat 5989319 5988645 DNA replication, recombination, modificat 5989319 5988645 DNA replication, recombination, modificat 5989319 5988645 DNA replication, recombination, modificat 5989459 5990667 Nucleotide biosynthesis and metabolism 5990675 5991130 Hypothetical, unclassified, unknown 5996035 5996985 Energy metabolism 6000142 5999753 Hypothetical, unclassified, unknown 6001377 6000760 Nucleotide biosynthesis and metabolism 6002039 6001398 Hypothetical, unclassified, unknown 6003329 6002958 Transcription, RNA processing and degra 6004095 6003376	Hypothetical unclassified unknown		5895260
Energy metabolism Hypothetical, unclassified, unknown Hypothetical, unclassified, unknown Biosynthesis of cofactors, prosthetic grou Biosynthesis of cofactors, prosthetic grou Hypothetical, unclassified, unknown Hypothetical, unclassified, unknow	Transcription RNA processing and degra		5898864
Hypothetical, unclassified, unknown 5907389 5907862 Hypothetical, unclassified, unknown 5908329 5907847 Biosynthesis of cofactors, prosthetic grou 5921496 5920741 Biosynthesis of cofactors, prosthetic grou 5922434 5921493 Hypothetical, unclassified, unknown 5941081 5940746 Cell wall / LPS / capsule 5941335 5941475 Amino acid biosynthesis and metabolism 5942744 5943574 Putative enzymes 5945234 5945932 Central intermediary metabolism 5952820 5952482 DNA replication, recombination, modificat 5962715 5964724 Energy metabolism 5969764 5969354 Hypothetical, unclassified, unknown 5972202 5971849 Translation, post-translational modification 5986118 5985882 DNA replication, recombination, modificat 5989319 5986645 DNA replication, recombination, modificat 5989459 5990667 Nucleotide biosynthesis and metabolism 5990075 5991130 Hypothetical, unclassified, unknown 5990035 5996985 Energy metabolism 6000142 5999753 Hypothetical, unclassified, unknown 6001377 6000760 Nucleotide biosynthesis and metabolism 6002039 6001398 Hypothetical, unclassified, unknown 6003329 6002958 Transcription, RNA processing and degra 6004095 6003376	Energy metabolism		5900368
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Biosynthesis of cofactors, prosthetic grou 5922434 5921493 Hypothetical, unclassified, unknown 5941081 5940746 Cell wall / LPS / capsule 5941335 5941475 Amino acid biosynthesis and metabolism 5942744 5943574 Putative enzymes 5945234 5945932 Central intermediary metabolism 5952820 5952482 DNA replication, recombination, modificat 5962715 5964724 Energy metabolism 5969764 5969354 Hypothetical, unclassified, unknown 5972202 5971849 Translation, post-translational modificat 5986118 5985882 DNA replication, recombination, modificat 5989319 5988645 DNA replication, recombination, modificat 5989319 5988645 DNA replication, recombination, modificat 5989459 5990667 Nucleotide biosynthesis and metabolism 5990675 5991130 Hypothetical, unclassified, unknown 5996035 5996985 Energy metabolism 6000142 5999753 Hypothetical, unclassified, unknown 6001377 6000760 Nucleotide biosynthesis and metabolism 6002039 6001398 Hypothetical, unclassified, unknown 6003329 6002958 Transcription, RNA processing and degra 6004095 6003376	Riosynthesis of cofactors prosthetic grou	5921496	5920741
Hypothetical, unclassified, unknown Cell wall / LPS / capsule Amino acid biosynthesis and metabolism Putative enzymes Central intermediary metabolism DNA replication, recombination, modificat Energy metabolism Translation, post-translational modificat DNA replication, recombination, modificat DNA replication, recombination, modificat DNA replication, recombination, modificat DNA replication, recombination, modificat DNA replication, recombination, modificat DNA replication, recombination, modificat DNA replication, recombination, modificat DNA replication, recombination, modificat DNA replication, recombination, modificat DNA replication, recombination, modificat DNA replication, recombination, modificat S989319 S988645 DNA replication, recombination, modificat S989459 S990667 Nucleotide biosynthesis and metabolism Hypothetical, unclassified, unknown S996035 S996985 Energy metabolism Hypothetical, unclassified, unknown Nucleotide biosynthesis and metabolism Hypothetical, unclassified, unknown Nucleotide biosynthesis and metabolism Hypothetical, unclassified, unknown Formula 15940746 S941335 S941374 S945932 S969764 S969354 S989319 S988645 S989319 S988645 S989319 S988645 S9990675 S991130 Hypothetical, unclassified, unknown G0001377 G000760 Nucleotide biosynthesis and metabolism Hypothetical, unclassified, unknown G003329 G002958 Transcription, RNA processing and degra G004095 G003376	Biosynthesis of cofactors prosthetic group		5921493
Cell wall / LPS / capsule59413355941475Amino acid biosynthesis and metabolism59427445943574Putative enzymes59452345945932Central intermediary metabolism59528205952482DNA replication, recombination, modificat59627155964724Energy metabolism59697645969354Hypothetical, unclassified, unknown59722025971849Translation, post-translational modification59861185985882DNA replication, recombination, modificat59893195986455DNA replication, recombination, modificat59894595990667Nucleotide biosynthesis and metabolism59906755991130Hypothetical, unclassified, unknown59960355996985Energy metabolism6001425999753Hypothetical, unclassified, unknown60013776000760Nucleotide biosynthesis and metabolism60020396001398Hypothetical, unclassified, unknown60033296002958Transcription, RNA processing and degra60040956003376	Hypothetical unclassified unknown		5940746
Amino acid biosynthesis and metabolism 5942744 5943574 Putative enzymes 5945234 5945932 Central intermediary metabolism 5952820 5952482 DNA replication, recombination, modificat 5962715 5964724 Energy metabolism 5969764 5969354 Hypothetical, unclassified, unknown 5972202 5971849 Translation, post-translational modification 5986118 5985882 DNA replication, recombination, modificat 5989319 5988645 DNA replication, recombination, modificat 5989459 5990667 Nucleotide biosynthesis and metabolism 5990675 5991130 Hypothetical, unclassified, unknown 5996035 5996985 Energy metabolism 6000142 5999753 Hypothetical, unclassified, unknown 6001377 6000760 Nucleotide biosynthesis and metabolism 6002039 6001398 Hypothetical, unclassified, unknown 6003329 6002958 Transcription, RNA processing and degra 6004095 6003376	Cell well / LPS / cansule		5941475
Putative enzymes 5945234 5945932 Central intermediary metabolism 5952820 5952482 DNA replication, recombination, modificat 5962715 5964724 Energy metabolism 5969764 5969354 Hypothetical, unclassified, unknown 5972202 5971849 Translation, post-translational modification 5986118 5985882 DNA replication, recombination, modificat 5989319 5988645 DNA replication, recombination, modificat 5989459 5990667 Nucleotide biosynthesis and metabolism 5990675 5991130 Hypothetical, unclassified, unknown 5996035 5996985 Energy metabolism 6000142 5999753 Hypothetical, unclassified, unknown 6001377 6000760 Nucleotide biosynthesis and metabolism 6002039 6001398 Hypothetical, unclassified, unknown 6003329 6002958 Transcription, RNA processing and degra 6004095 6003376	Amino acid biosynthesis and metabolism		5943574
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Energy metabolism 5969764 5969354 Hypothetical, unclassified, unknown 5972202 5971849 Translation, post-translational modification 5986118 5985882 DNA replication, recombination, modificat 5989319 5988645 DNA replication, recombination, modificat 5989459 5990667 Nucleotide biosynthesis and metabolism 5990675 5991130 Hypothetical, unclassified, unknown 5996035 5996985 Energy metabolism 6000142 5999753 Hypothetical, unclassified, unknown 6001377 6000760 Nucleotide biosynthesis and metabolism 6002039 6001398 Hypothetical, unclassified, unknown 6003329 6002958 Transcription, RNA processing and degra 6004095 6003376	DNA replication recombination modifica		5964724
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Translation, post-translational modification 5986118 5985882 DNA replication, recombination, modificat 5989319 5988645 DNA replication, recombination, modificat 5989459 5990667 Nucleotide biosynthesis and metabolism 5990675 5991130 Hypothetical, unclassified, unknown 5996035 5996985 Energy metabolism 6000142 5999753 Hypothetical, unclassified, unknown 6001377 6000760 Nucleotide biosynthesis and metabolism 6002039 6001398 Hypothetical, unclassified, unknown 6003329 6002958 Transcription, RNA processing and degra 6004095 6003376	Hypothetical unclassified unknown		
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Nucleotide biosynthesis and metabolism 5990675 5991130 Hypothetical, unclassified, unknown 5996035 5996985 Energy metabolism 6000142 5999753 Hypothetical, unclassified, unknown 6001377 6000760 Nucleotide biosynthesis and metabolism 6002039 6001398 Hypothetical, unclassified, unknown 6003329 6002958 Transcription, RNA processing and degra 6004095 6003376	DNA replication, recombination, modification		
Hypothetical, unclassified, unknown 5996035 5996985 Energy metabolism 6000142 5999753 Hypothetical, unclassified, unknown 6001377 6000760 Nucleotide biosynthesis and metabolism 6002039 6001398 Hypothetical, unclassified, unknown 6003329 6002958 Transcription, RNA processing and degra 6004095 6003376	Nucleotide biosynthesis and metabolism	5990675	
Energy metabolism 6000142 5999753 Hypothetical, unclassified, unknown 6001377 6000760 Nucleotide biosynthesis and metabolism 6002039 6001398 Hypothetical, unclassified, unknown 6003329 6002958 Transcription, RNA processing and degra 6004095 6003376	Hypothetical unclassified unknown		
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Hypothetical, unclassified, unknown 6003329 6002958 Transcription, RNA processing and degra 6004095 6003376	nypotnetical, unclassified, unknown		
Transcription, RNA processing and degra 6004095 6003376	NUCleotide piosynthesis and metabolish		
I I all Scription, The Cooper in grant cog.	Hypothetical, unclassified, unknown		
Hypothetical, unclassified, unknown 0004270 0000100	Transcription, KINA processing and degi	6004030	
	Hypothetical, unclassified, unknown	3004270	, 0000.00

Nucleotide biosynthesis and metabolism	6005198	6005809
Hypothetical, unclassified, unknown	6008397	6008777
Hypothetical, unclassified, unknown	6017013	6016621
Carbon compound catabolism	6018996	6018829
Carbon compound catabolism	6019347	6019180
Biosynthesis of cofactors, prosthetic grou	6025304	6026194
Two-component regulatory systems	6032267	6031365
Hypothetical, unclassified, unknown	6060199	6059822
Hypothetical, unclassified, unknown	6063831	6063352
Putative enzymes	6069098	6067944
Hypothetical, unclassified, unknown	6074229	6075206
Transcriptional regulators	6082866	6083072
Hypothetical, unclassified, unknown	6083104	6083508
Hypothetical, unclassified, unknown	6083752	6084084
Hypothetical, unclassified, unknown	6084544	6084368
Carbon compound catabolism	6096706	6097026
Hypothetical, unclassified, unknown	6148318	6149181
Hypothetical, unclassified, unknown	6151313	6151525
Hypothetical, unclassified, unknown	6155202	6154783
Hypothetical, unclassified, unknown	6158178	6158942
Translation, post-translational modification	- 5	6158948
Hypothetical, unclassified, unknown	6171732	6171926
Hypothetical, unclassified, unknown	6172872	6172711
Hypothetical, unclassified, unknown	6188854	6188165
Transport of small molecules	6195308	6196315
Hypothetical, unclassified, unknown	6219068	6218856
Transport of small molecules	6221100	6222857
Transport of small molecules	6225924	6224896
Hypothetical, unclassified, unknown	6227081	6227449
Hypothetical, unclassified, unknown	6228243	6227602
Hypothetical, unclassified, unknown	6236228	6235830
Central intermediary metabolism	6244945	6243110
Cell wall / LPS / capsule	6247689	6246325
Energy metabolism	6248235	6247810
Energy metabolism	6249653	6248277
Energy metabolism	6250544	6249684
Energy metabolism	6252139	6250595
Energy metabolism	6252694	6252158
Energy metabolism	6253176	6252706
Energy metabolism	6253491	6253234
	6254410	6253541
Energy metabolism	6254807	6254427
Energy metabolism Cell division	6255843	625497
Hypothetical, unclassified, unknown	6260053	6259670
	6263563	6261827
Hypothetical, unclassified, unknown Translation, post-translational modificatio		6263804
Translation, post-translational modification		6264226
Translation, post-translational modificatio	0204300	0204220

蘇 Ra新D菜	e intlengible		Genername
4269	4200	0.9999719	rpoC
4270	4074	0.9999719	rpoB 1
3640	3522	0.9999058	dnaE ;
1156	2892	0.9995054	nrdA
3834	2853	0.9994519	valS
4560	2832	0.9994208	ileS
595	2775	0.999327	ostA
3168	2772	0.9993217	. gyrA
4403	2751	0.9992831	secA
903,	2625	0.9990012	alaS
3987	2622	0.9989933	leuS
1787	2610	0.998961	acnB .
3011	2607	0.9989528	topA
4744	2523	0.9986937	infB
2615	2436	0.9983575	ftsK
4	2421	0.9982914	gyrB
1803	2397	0.99818	lon
3648	2394	0.9981655	
. 1529	2385	0.9981216	lig
2739	2379	0.9980917	pheT
3704	2310	0.9977116	
4964	2265	0.9974239	parC
5050	2220	0.9971	priA
260	2151	0.9965225	
1372	2136	0.9963824	
2071	2109	0.996116	fusA2
4740	2106	0.9960852	pnp
8	2055	0.9955228	glyS
1532	2046	0.9954155	dnaX
3482	2034	0.9952684	metG
5296	2010	0.9949599	rep
1939	1998	0.9947981	
1480	1974	0.9944589	ccmF
5072	1944	0.9940037	
2744	1923	0.9936629	thrS
1068	1911	0.9934596	
1596	1905	0.9933555	htpG
3157	1890	0.9930879	
4967	1890	0.9930879	parE
4044	1884	0.9929779	dxs
1370	1866	0.9926372	
3821	1863	0.9925788	secD
3810	1860	0.99252	hscA
1810	1848	0.99228	
5549	1836	0.9920322	glmS
4997	1812	0.9915127	msbA
767	1800	0.9912404	lepA
5187	1791	0.9910304	
1583	1773	0.9905952	sdhA
5051	1764	0.9903698	argS
5529	1758	0.9902165	<u> </u>
			•

	1758	0.9902165	
3460	1740	0.9897418	ftsl
4418	1737	0.9896605	
5568 : 2298	1737	0.9893287	
	1725	0.9893287	ilvl
4696	1716	0.9890729	recJ
3725	1716	0.9890729	proS
956	1710	0.9886329	ureC
4868	1701	0.9886329	pilB
4526		0.9879869	rpsA
3162	1680	0.9879809	glnS
1794	1671	0.9875032	pgi
4732	1665	0.9874041	pgi pgi
2075	1662	0.9872036	
2953	1656	1	groEL
4385	1644	0.986793	
3637	1629	0.9862612	pyrG
1251	1626	0.9861522	atsA
183	1611	0.9855946	aisA
5065	1602	0.9852493	auc A
3769	1578	0.9842875	, guaA
2818	1578	0.9842875	
3024	1560	0.9835251	
5131	1548	0.9829965	pgm
1331	1548	0.9829965	dnaA
1	1545	0.9828617	
5556	1545	0.9828617	atpA
4961	1539	0.9825889	Int
3984	1536	0.9824509	Int
2207	1521	0.9817442	tiV
2343	1509	0.9811584	mtlY
3103	1509	0.9811584	xcpR
1820	1503	0.9808585	nhaB
985	1497	0.9805538	<u> </u>
3570	1494	0.9803997	mmsA
4462	1494	0.9803997	rpoN
443	1491	0.9802443	nusA
4745	1482	0.9797707	HusA
5006	1479	0.9796104	
2097	1476	0.9794487	
5237	1467	0.9789561	murE
4417	1464	0.9787893	IIIui⊏
2037	1461	0.9786211	
202	1458	0.9784516	on the
427	1458	0.9784516	oprM
2521	1455	0.9782808	czcB gatA
4483	1455	0.9782808	
4329	1452	0.9781087	pykA matE
913	1449	0.9779351	mgtE
4484	1446	0.9777602	gatB
4411	1443	0.9775839	murC
1587	1437	0.9772271	lpdG
2073	1431	i 0.9768646	

2002	1425	0.9764964	
2391 ;	1425 <u>:</u>	0.9764964	·
1551	1416	0.975933	
5119	1410	0.9755499	glnA
686	1410	0.9755499	·
3876	1407	0.9753561	narK2
704	1395	0.9745653	
2991	1395 :	0.9745653	sth
4931	1395	0.9745653	dnaB
3001	1386	0.9739556	
1795	1383	0.9737491	cysS
3777	1380	0.973541	xseA
4416	1377	0.9733313	murF
5554	1377	0.9733313	atpD
3746	1374	0.9731199	ffh
2629	1371	0.9729068	purB
<u></u>	1368	0.972692	ftsY
373	1368	0.972692	
1217	1368	0.972692	
3081	1362	0.9722573	
2131	1350	0.9713671	:
2729		0.9713671	
119	1350	0.9713671	accC
4848	1350	0.9711402	trpS
4439	1347	0.9711402	murD
4414	1347	0.9711402	nuoF
2641	1347	0.9711402	11401
2843	1347	0.9711402	
2336	1341	1	pilR
4547	1338	0.9704484	glmM
4749	1338	0.9704484	pepP
5224	1335	0.9702141	hehr
2475	1335	0.9702141	
3638	1329	0.96974	secY
4243	1329	0.96974	SECT
716	1326	0.9695001	
2214	1323	0.9692583	
2794	1317	0.968769	
4887	1317	0.968769	ļ
3280	1317	0.968769	оргО
3154	1317	0.968769	wzy
2539	1314	0.9685214	
3159	1311	0.9682719	wbpA
2338	1311	0.9682719	1
1183	1311	0.9682719	dctA
1120	1308	0.9680204	
4099	1305	0.9677669	
2986	1302	0.9675113	
972	1299	0.9672538	tolB
2734	1296	0.9669942	<u> </u>
4938	1293	0.9667326	l purA
594	1293	0.9667326	surA
3635	1290	0.9664688	eno
	<u> </u>		

	4007	0.966203	
1215	1287	0.9659351	hemL
3977	1284	0.9656651	serS
2612	1281		waaA
4988	1278		waan
1895	1275	0.9651185 0.9645633	fabF2
1373	1269 ,	0.9645633	hemA
4666	1269		murA
4450	1266	0.9642824	IIIuiA
1951	1266	0.9642824	rho
5239	1260	0.9637139 0.9631363	ftsA
4408	1254		115/4
2080	1251	0.9628441	
2988	1251	0.9628441	n rdD
1155	1248	0.9625495	nrdB
3147	1242	0.9619534	wbpJ
1488	1239	0.9616518	1
904	1239	0.9616518	lysC
3153	1236	0.9613478	WZX
3733	1230	0.9607326	
1595	1230	0.9607326	
2042	1230	0.9607326	
1914	1227	0.9604213	
2500	1227	0.9604213	
446	1224	0.9601075	
4008	1224	0.9601075	<u> </u>
2928	1224	0.9601075	
4566	1221	0.9597913	obg
5221	1218	0.9594726	
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0104		,	

4040		0.8398864	
4916	696	0.8398864	
2105	696		<u> </u>
5052	696	0.8398864	tolQ
969	696	0.8398864	1010
1894	693	0.8386172	
2280	693	0.8386172	
213	693	0.8386172	
733	693	0.8386172	
3163	690	0.8373379	cmk
5496	690	0.8373379	
4885	690	0.8373379	irlR
4257	687	0.8360484	rpsC
2719	687	0.8360484	
120	687	0.8360484	
504	687	0.8360484	bioD
1862	687	0.8360484	modB
. 527	684	0.8347487	dnr
1118	684	0.8347487	
2987	684	0.8347487	
2617	681	0.8334387	aat
3685	681	0.8334387	•
2638	678	0.8321183	nuoB
1980	678	0.8321183	
2034	675	0.8307875	
1261	675	0.8307875	
2996	675	0.8307875	ngrD
3528	675	0.8307875	rnt
453	675	0.8307875	
976	675	0.8307875	
5319	675	0.8307875	radC
607	675	0.8307875	rpe
2284	672	0.8294461	
1167	672	0.8294461	
1476	672	0.8294461	ccmB
1193	672	0.8294461	
4892	672	0.8294461	ureF
330	672	0.8294461	rpiA
944	669	0.8280941	purN
1269	669	0.8280941	
243	669	0.8280941	
167	666	0.8267314	
65	666	0.8267314	T
4029	666	0.8267314	T
3368	666	0.8267314	1
1978	666	0.8267314	
4776	666	0.8267314	1
1623	663	0.8253578	
3181	663	0.8253578	
3890	663	0.8253578	
	663	0.8253578	
1090	663	0.8253578	1
697	660	0.8239734	
1526	1 000	1 0.0233134	

		0.0000724	
2782	660 !	0.8239734	
3110	660	0.8239734	-1.0
4055	660	0.8239734	ribC
4121	660	0.8239734	
2832	657	0.822578	tpm
2351 '	654	0.8211715	i
3550	651	0.8197539	algF
4998	651	0.8197539	
4757	651	0.8197539	
1504	651	0.8197539	
1049	648	0.818325	pdxH
655	648	0.818325	
2222	648	0.818325	
3859	648	0.818325	
2257	648	0.818325	pvcD
3973	648	0.818325	
4676	648	0.818325	
4453	648	0.818325	
1905	648	0.818325	
4216	645	0.8168848	
4006	645	0.8168848	· · ·
2473	645	0.8168848	
1825	645	0.8168848	
652	645	0.8168848	vfr
251	642	0.8154332	
5331	642	0.8154332	pyrE
5142	642	0.8154332	hisH1
5534	642	0.8154332	
3730	642	0.8154332	ļi
	639	0.8139701	maiA
2007	639	0.8139701	
2720	639	0.8139701	
	639	0.8139701	upp
4646	639	0.8139701	
826	639	0.8139701	nth
3495	639	0.8139701	
3678	639	0.8139701	
3450	639	0.8139701	
2066	639	0.8139701	
990	639	0.8139701	
4182	636	0.8124954	
2983	636	0.8124954	rluA
3246	636	0.8124954	1
114		0.8124954	rplC
4263	636	0.8124954	1 - 12:3
2126	636	0.811009	
4507	633	0.811009	-
1558	633	0.811009	
1397	633	0.811009	tmk
2962	633		- UIIK
4890	630	0.8095108	+
629	630	0.8095108	+
4019	630	0.8095108	

4440 !	630	0.8095108	
	627	0.8080008	
3232		0.8080008	lolA .
2614	627	0.8080008	101/4 .
5064	627	0.8064788	
853	624		
3665	624	0.8064788	
1790 :	624	0.000 11 00	#a.l
4752	024	0.0004700	ftsJ
981	624	0.8064788	
3988	624	0.8064788	
5341	621	0.8049447	
4239	621	0.8049447	rpsD
1757	618	0.8033984	thrH
2504	618	0.8033984	
4668	618	0.8033984	
4428 1	618	0.8033984	sspA
5330	618	0.8033984	
4047	618	0.8033984	ribA
2807	618	0.8033984	
3407	618	0.8033984	hasAp
1315	615	0.8018399	
5470	615	0.8018399	
4671	615	0.8018399	
1219	615	0.8018399	
571	615	0.8018399	
4871	615	0.8018399	
3754	612	0.800269	
3354	612	0.800269	
4529	612	0.800269	
5336	612	0.800269	gmk
3152	609	0.7986857	hisH2
1962	609	0.7986857	
2459	606	0.7970898	
154	606	0.7970898	pcaG
2602	606	0.7970898	
1432	606	0.7970898	lasl
3326	606	0.7970898	
377	606	0.7970898	
4262	603	0.7954813	rpiD
1089	603	0.7954813	<u> </u>
5190	603	0.7954813	
3273	600	0.7938601	
2451	600	0.7938601	
3472	597	0.7922259	
370	597	0.7922259	
3030	597	0.7922259	
2792	597	0.7922259	
1172	597	0.7922259	napC
3446	594	0.7905789	
4012	594	0.7905789	
2916	594	0.7905789	
4425	594	0.7905789	

684	594	0.7905789	
4345	591 !	0.7889187	
4063	591	0.7889187	
3281	591	0.7889187	
3796	588	0.7872454	
2774	588	0.7872454	
4553	588	0.7872454	pilX
4923	588	0.7872454	
763	585	0.7855589	mucA
2196	585	0.7855589	
3765	585	0.7855589	
1847	585	0.7855589	
3489	585	0.7855589	
3414	585	0.7855589	
4672	585	0.7855589	
1280	585	0.7855589	····
4366	582	0.7838589	sodB
2936	582	0.7838589	
3255	579	0.7821455	
1785	579	0.7821455	
111	579	0.7821455	
358	579	0.7821455	
3867	576	0.7804185	
3156	576	0.7804185	wbpD
776	573	0.7786779	
3784	573	0.7786779	
4894	573	0.7786779	
4459	573	0.7786779	
2372	573	0.7786779	
2910	570	0.7769234	
1928	570	0.7769234	rimJ
475	570	0.7769234	
1955	570	0.7769234	
422	570	0.7769234	
405	570	0.7769234	
2851	567	0.775155	efp
5176	567	0.775155	
1994	564	0.7733726	
4600	564	0.7733726	nfxB
4499	564	0.7733726	
4171	564	0.7733726	
139	564	0.7733726	ahpC
3227	564	0.7733726	ppiA
1427	564	0.7733726	
2331	561	0.7715761	
2406	561	0.7715761	
3438	561	0.7715761	folE1
4831	561	0.7715761	
4762	561	. 0.7715761	grpE
2584	561	0.7715761	pgsA
1204	558	0.7697653	<u> </u>
1675	558	i 0.7697653	
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3653 558 0.7697653 ITT 22 558 0.7697653 3291 555 0.7679402 525 555 0.7679402 525 555 0.7679402 1472 555 0.7679402 1472 555 0.7679402 1472 555 0.7679402 1472 555 0.7679402 1472 555 0.7679402 1472 1543 552 0.7661006 kdpC 1635 1552 0.7661006 kdpC 1635 152 0.7661006 kdpC 1635 1635 152 0.7661006 kdpC 1635 154 1549 0.7642464 3767 549 0.7642464 3767 549 0.7642464 3767 549 0.7623775 rmIC 1543 549 0.7623775 rmIC 2434 546 0.7623775 rmIC 2434 546 0.7623775 foll22 171 543 0.7604938 ccmG 3726 540 0.7685952 rplE 1768 540 0.7585952 rplE <				
2784 558 0.7697653 3291 555 0.7679402 5225 555 0.7679402 535 555 0.7679402 1472 555 0.7679402 311 555 0.7679402 311 555 0.7679402 311 555 0.7679402 311 555 0.7661006 infC 1635 552 0.7661006 kdpC 1884 552 0.7661006 kdpC 1884 552 0.7661006 kdpC 1884 552 0.7661006 kdpC 1884 552 0.7661006 kdpC 1884 552 0.7661006 kdpC 1884 552 0.7661006 kdpC 1884 552 0.7661006 kdpC 1884 552 0.7661006 kdpC 1884 552 0.7661006 kdpC 1884 552 0.7661006 kdpC 1884 549 0.7642464 apt 2865 546 0.7623775 rmIC 2865 546 0.7623775 rmIC 2875 548 0.7623775 rmIC 2875 548 0.7623775 folE2 149 546 0.7623775 folE2 171 543 0.7604938 ccmG 171 543 0.7604938 ccmG 171 543 0.7604938 ccmG 172 540 0.7585952 rpIE 1768 540 0.7585952 rpIE 1768 540 0.7585952 rpIE 1768 540 0.7585952 rpIE 1768 540 0.7586815 atpH 1875 537 0.7566815 atpH 1885 537 0.7566815 atpH 1877 534 0.7547527 rpIF	3653	558	0.7697653	frr
3291 555 0.7679402 525 555 0.7679402 535 555 0.7679402 535 555 0.7679402 531 555 0.7679402 531 555 0.7679402 5311 555 0.7661006 infC 635 552 0.7661006 kdpC 54 549 0.7642464 3767 549 0.7642464 3767 549 0.7642464 3767 549 0.7642464 3767 549 0.7642464 3767 549 0.7642464 3767 549 0.7623775 included a series of the content of the con	22			
5225 555 0.7679402 535 555 0.7679402 1472 555 0.7679402 311 555 0.7661006 infC 1635 552 0.7661006 kdpC 1884 552 0.7661006 kdpC 1884 552 0.7661006 kdpC 54 549 0.7642464 apt 3767 549 0.7642464 apt 1543 549 0.7642464 apt 2365 546 0.7623775 rmIC 2434 546 0.7623775 rmIC 2434 546 0.7623775 folE2 171 543 0.7604938 ccmG 149 546 0.7623775 folE2 171 543 0.7604938 ccmG 1481 543 0.7604938 ccmG 3726 540 0.7585952 rplE 1768 540 0.7585952 rplE	2784			
535 555 0.7679402 1472 555 0.7679402 311 555 0.7661006 infC 1635 552 0.7661006 kdpC 1884 552 0.7661006 kdpC 1884 552 0.7661006 kdpC 54 549 0.7642464 apt 3767 549 0.7642464 apt 2365 546 0.7623775 rmIC 543 549 0.7642464 apt 2365 546 0.7623775 rmIC 546 0.7623775 rmIC 2434 546 0.7623775 rmIC 149 546 0.7623775 folE2 171 543 0.7604938 ccmG 3726 540 0.7585952 rplE 4251 540 0.7585952 rplE 4768 540 0.7585952 rplE 6 537 0.7566815 atpH				
1472 555 0.7679402 311 555 0.7661006 infC 1635 552 0.7661006 kdpC 1884 552 0.7661006 kdpC 1884 552 0.7661006 kdpC 54 549 0.7642464 apt 3767 549 0.7642464 apt 1543 549 0.7642464 apt 2365 546 0.7623775 rmIC 5164 546 0.7623775 rmIC 2434 546 0.7623775 rmIC 149 546 0.7623775 folE2 171 543 0.7604938 ccmG 174 543 0.7604938 ccmG 3726 540 0.7585952 rplE 1768 540 0.7585952 rplE 937 540 0.7586952 rplE 937 540 0.7586915 atpH 3396 537 0.7566815				
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2743 552 0.7661006 infC 1635 552 0.7661006 kdpC 1884 552 0.7661006 kdpC 54 549 0.7642464 3767 549 0.7642464 3767 549 0.7642464 apt 2365 546 0.7623775 rmIC 1543 549 0.7623775 rmIC 2434 546 0.7623775 rmIC 2434 546 0.7623775 rmIC 149 546 0.7623775 foIE2 171 543 0.7604938 ccmG 171 543 0.7604938 ccmG 3726 540 0.7585952 rpIE 1768 540 0.7585952 rpIE 1768 540 0.7585952 rpIE 6 537 0.7566815 atpH 3396 537 0.7566815 atpH 3396 537 0.7566815 atpH 4841 537 0.7566815 atpH 377 534 </td <td>1472</td> <td>555</td> <td></td> <td></td>	1472	555		
1635 552 0.7661006 kdpC 1884 552 0.7661006 54 549 0.7642464 3767 549 0.7642464 1543 549 0.7642464 2365 546 0.7623775 5164 546 0.7623775 5164 546 0.7623775 149 546 0.7623775 149 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 171 543 0.7604938 ccmG 3726 540 0.7585952 4251 540 0.7585952 4251 540 0.7585952 937 540 0.7585952 937 540 0.7585952 937 540 0.7586815 5557 537 0.7566815 5557 537 0.7566815 4841 537 0.7566815 4841 537 0.7566815 4841 537 0.7566815 4841 537 0.7566815 4841 537 0.7566815 4842 534 0.7547527 1885 534 0.7547527 1885 534 0.7547527 1885 534 0.7547527 1885 534 0.7547527 1885 534 0.7547527 1885 534 0.7547527 1885 534 0.7547527 1869 534 0.7547527 1870 534 0.7547527 1885 534 0.7547527 1885 534 0.7547527 1886 534 0.7547527 1887 534 0.7547527 1888 534 0.7547527 1889 534 0.7547527 1880 534 0.7547527 1880 534 0.7547527 1880 534 0.7547527 1881 534 0.7547527 1885 534 0.7547527 1886 534 0.7547527 1887 538 0.750849 1300 528 0.750849 1300 528 0.750849 2733 528 0.750849 2733 528 0.750849 3905 528 0.750849 3744 528 0.750849 3744 528 0.750849 3744 528 0.750849 514 525 0.7488739 nirL	311	555		
1884 552 0.7661006 54 549 0.7642464 3767 549 0.7642464 1543 549 0.7623775 5164 546 0.7623775 5164 546 0.7623775 149 546 0.7623775 149 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 543 0.7604938 1481 543 0.7604938 3726 540 0.7585952 4251 540 0.7585952 937 540 0.7585952 937 540 0.7585952 937 540 0.7585952 937 540 0.7585952 937 540 0.7586815 3396 537 0.7566815 4841 537 0.7566815 <t< td=""><td>2743</td><td>552</td><td></td><td></td></t<>	2743	552		
54 549 0.7642464 3767 549 0.7642464 1543 549 0.7623775 5164 546 0.7623775 5164 546 0.7623775 149 546 0.7623775 149 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7585952 171 543 0.7586952	1635	552		kdpC
3767 549 0.7642464 apt 1543 549 0.7642464 apt 2365 546 0.7623775 rmIC 5164 546 0.7623775 rmIC 2434 546 0.7623775 folE2 149 546 0.7623775 folE2 171 543 0.7604938 ccmG 3726 540 0.7585952 rplE 4251 540 0.7585952 rplE 1768 540 0.7585952 rplE 937 540 0.7585952 rplE 6 537 0.7566815 atpH 3396 537 0.7566815 atpH 3396 537 0.7566815 nosL 4841 537 0.7566815 atpH 4962 537 0.7566815 rplF 4962 537 0.7547527 rplF 1377 534 0.7547527 rplF 4275 534	1884	552		
1543 549 0.7642464 apt 2365 546 0.7623775 rmIC 5164 546 0.7623775 rmIC 2434 546 0.7623775 rmIC 149 546 0.7623775 foIE2 1674 546 0.7623775 foIE2 171 543 0.7604938 ccmG 3726 540 0.7585952 rpIE 4251 540 0.7585952 rpIE 1768 540 0.7585952 rpIE 1768 540 0.7585952 rpIE 937 540 0.7586952 rpIE 1768 540 0.7586952 rpIE 1768 540 0.7586952 rpIE 1768 540 0.7586952 rpIE 1768 540 0.7586952 rpIE 3376 537 0.7566815 atpH 3396 537 0.7566815 nosL 4841 537 </td <td>54</td> <td>549</td> <td></td> <td></td>	54	549		
2365 546 0.7623775 5164 546 0.7623775 149 546 0.7623775 149 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1674 546 0.7623775 1675 543 0.7604938 1481 543 0.7604938 ccmG 3726 540 0.7585952 4251 540 0.7585952 1768 540 0.7585952 937 540 0.7585952 6 537 0.7566815 5557 537 0.7566815 3396 537 0.7566815 2971 537 0.7566815 2971 537 0.7566815 4841 537 0.7566815 2971 537 0.7566815 4962 537 0.7566815 4248 534 0.7547527 1885 534 0.7547527 1885 534 0.7547527 1885 534 0.7547527 1886 534 0.7547527 1887 534 0.7547527 1888 534 0.7547527 1885 534 0.7547527 1886 534 0.7547527 1887 534 0.7547527 1888 534 0.7547527 1885 534 0.7547527 1886 534 0.7547527 1887 534 0.7547527 1888 534 0.7547527 1889 534 0.7547527 1898 534 0.754	3767	549		
2365 546 0.7623775 rmIC 5164 546 0.7623775 rmIC 2434 546 0.7623775 rmIC 149 546 0.7623775 foIE2 1674 546 0.7604938 ccmG 171 543 0.7604938 ccmG 3726 540 0.7585952 rpIE 4251 540 0.7585952 rpIE 1768 540 0.7585952 rpIE 937 540 0.7585952 rpIE 1768 540 0.7586952 rpIE 3370 0.7566815 atpH 3396 537 0.7566815 nosL 4841 537 0.756		549	0.7642464	apt
5164 546 0.7623775 rmlC 2434 546 0.7623775 149 546 0.7623775 1674 546 0.7623775 folE2 171 543 0.7604938 ccmG 171 543 0.7604938 ccmG 3726 540 0.7585952 rplE 1768 540 0.7585952 rplE 4251 540 0.7585952 rplE 1768 540 0.7585952 rplE 937 540 0.7585952 rplE 6 537 0.7566815 atpH 3396 537 0.7566815 atpH nosL 4841 537 0.7566815 nosL 4841 537 0.7566815 10.7547527 rplF 4962 537 0.7566815 0.7547527 rplF 1377 534 0.7547527 rplF 1377 534 0.7547527 rplF 1885 534 0.7547527 nusG 4649 534 0.7547527		546		
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149 546 0.7623775 folE2 1674 546 0.7623775 folE2 171 543 0.7604938 ccmG 3726 540 0.7585952 rplE 4251 540 0.7585952 rplE 1768 540 0.7585952 rplE 937 540 0.7585952 rplE 6 537 0.7566815 atpH 3396 537 0.7566815 nosL 4841 537 0.7566815 nosL 4841 537 0.7566815 nosL 4962 537 0.7566815 rplF 1377 534 0.7547527 rplF 1377 534 0.7547527 rplF 1377 534 0.7547527 nusG 4649 534 0.7547527 nusG 4649 534 0.7547527 nusG 5111 531 0.7528085 gloA3 4765 531 <td></td> <td></td> <td>0.7623775</td> <td></td>			0.7623775	
1674 546 0.7623775 folE2 171 543 0.7604938 ccmG 3726 540 0.7585952 rplE 4251 540 0.7585952 rplE 1768 540 0.7585952 rplE 937 540 0.7585952 stpH 6 537 0.7566815 stpH 3396 537 0.7566815 nosL 4841 537 0.7566815 nosL 4962 537 0.7566815 rplF 1377 534 0.7547527 rplF 1377 534 0.7547527 rplF 1377 534 0.7547527 nusG 4649 534 0.7547527 nusG 4649 534 0.7547527 nusG 1154 534 0.7547527 nusG 531 0.7528085 gloA3 4765 531 0.7528085 omlA 3575 531 0.75084		546	0.7623775	
171 543 0.7604938 ccmG 3726 540 0.7585952 rplE 4251 540 0.7585952 rplE 1768 540 0.7585952 rplE 937 540 0.7585952 stplE 6 537 0.7566815 atpH 3396 537 0.7566815 nosL 4841 537 0.7566815 nosL 4841 537 0.7566815 nosL 4962 537 0.7566815 nosL 4962 537 0.7566815 rplF 4248 534 0.7547527 rplF 1377 534 0.7547527 rplF 1385 534 0.7547527 nusG 4248 534 0.7547527 nusG 4275 534 0.7547527 nusG 4275 534 0.7547527 nusG 5111 531 0.7528085 gloA3 4765 531 <td></td> <td></td> <td>0.7623775</td> <td>folE2</td>			0.7623775	folE2
1481 543 0.7604938 ccmG 3726 540 0.7585952 rplE 4251 540 0.7585952 rplE 1768 540 0.7585952 rplE 937 540 0.7585952 rplE 6 537 0.7566815 atpH 3396 537 0.7566815 atpH 3396 537 0.7566815 nosL 4841 537 0.7566815 nosL 4841 537 0.7566815 rplF 4962 537 0.7566815 rplF 4248 534 0.7547527 rplF 1377 534 0.7547527 rplF 1377 534 0.7547527 nusG 4649 534 0.7547527 nusG 4649 534 0.7547527 nusG 5111 531 0.7528085 gloA3 4765 531 0.7528085 omlA 3575 531 <td></td> <td></td> <td>0.7604938</td> <td></td>			0.7604938	
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	505	0.7488739	xcpZ
3095	525	0.7488739 0.7488739	xcpz
2136	525		
1134	522	0.7468831	
1062	522	0.7468831	
1442	522		
3693	522	0.7468831	- basD
3811 !	522	0.7468831 i	hscB ·
145 .	519	0.7448766	
1845	. 519	0.7448766	
3100	519	0.7448766	хсрU
4866	519	0.7448766	
5039	519	0.7448766	aroK
2496	516	0.7428542	
3911	516	0.7428542	
4050	516	0.7428542	pgpA
1610	516	0.7428542	fabA
3287	516	0.7428542	
403	513	0.7408157	pyrR
1514	510	0.7387611	
4114	510	0.7387611	
4559	510	0.7387611	IspA
47	510	0.7387611	
4104	510	0.7387611	
3965	510	0.7387611	
2184	510	0.7387611	
1912	507	0.7366902	
1657	507	0.7366902	
1666	507	0.7366902	
55	507	0.7366902	
3647	507	0.7366902	
973	507	0.7366902	
585	507	0.7366902	
2859	507	0.7366902	greB
350	507	0.7366902	folA
3288	504	0.7346029	
1967	501	0.732499	
4272	501	0.732499	rplJ
4246	501	0.732499	rpsE
3318	501	0.732499	
3756	501	0.732499	
2226	501	0.732499	
2645	501	0.732499	nuoJ
2367	498	0.7303785	
1837	498	0.7303785	
261	498	0.7303785	
4232	498	0.7303785	ssb
1035	495	0.7282411	
5128	492	0.7260868	secB
3815	492	0.7260868	
1173	492	0.7260868	napB
1176	492	0.7260868	napF
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5558 i	471	0.7105208	atpF
4267	471	0.7105208	rpsG
2052	471	0.7105208	cynS
4847	471	0.7105208	accB
962	471	0.7105208	
2171	471	0.7105208	
4948	468	0.7082261	
332	468	0:7082261	
4107	468	0.7082261	
1482	468	0.7082261	ccmH
4183	468	0.7082261	
2427	468	0.7082261	•.
2786	468	0.7082261	
953	465	0.7059131	
4564	465	0.7059131	
2731	465	0.7059131	
4464	465	0.7059131	ptsN
80	465	0.7059131	
4057	465	0.7059131	
2978	465	0.7059131	ptpA
1306	462	0.7035818	
3616	462	0.7035818	
1673	462	0.7035818	
	459	0.701232	
3470	459	0.701232	
3380	459	0.701232	
4746 5229	459	0.701232	
3320	456	0.6988636	
2499	456	0.6988636	
3309	456	0.6988636	
1	456	0.6988636	
4828	456	0.6988636	osmC
59	456	0.6988636	dut
5321	456	0.6988636	
4421	453	0.6964764	
4697	453	0.6964764	
2538	453	0.6964764	<u> </u>
2829	453	0.6964764	moaE
3916		0.6964764	111000
3435	453 453	0.6964764	
115	450	0.6940703	
578		0.6940703	
678	450	0.6940703	pilA
4525	450	0.6940703	- Pin (
1285	450	0.6940703	
614	450	0.6916451	
822	447	0.6916451	aroQ2
245	447		rnhA
1815	447	0.6916451	11111/
1594	447	0.6916451	-
4630	444	0.6892007	
1122	444	0.6892007	
3067	444	0.6892007	

1105	444	0.6892007	fliJ :
970 i	441	0.6867369	tolR
2982	441	0.6867369	
3645	441	0.6867369	fabZ
61	438	0.6842536	
1835	438	0.6842536	
5178	438	0.6842536	
1618	438	0.6842536	
2577	438	0.6842536	
3017	438	0.6842536	
2775	438	0.6842536	
1710	438	0.6842536	exsC
3341	435	0.6817506	
94	435	0.6817506	-
2436	435	0.6817506	
4244	435	0.6817506	rplO
	435	0.6817506	
2756	435	0.6817506	
404		0.6817506	
4610	435	0.6817506	
250	435	0.6817506	
4767	435		
433	435	0.6817506	
2675	435	0.6817506	
720	435	0.6817506	
679	432	0.6792278	ndk
3807	432	0.6792278	
4274	432	0.6792278	rplK
3986	432	0.6792278	
52	429	0.6766849	
4433	429	0.6766849	rplM
1560	429	0.6766849	
2282	429	0.6766849	
2120	429.	0.6766849	
4169	429	0.6766849	
5116	426	0.6741219	
2368	426	0.6741219	
2673	426	0.6741219	
700	426	0.6741219	
5553	426	0.6741219	atpC
2187	426	0.6741219	
3332	426	0.6741219	<u> </u>
4518	426	0.6741219	
2894	423	0.6715386	
653	423	0.6715386	
661	423	0.6715386	
542	420	0.6689348	
5130	420	0.6689348	
5465	420	0.6689348	
4935	420	0.6689348	rpsF
850	420	0.6689348	
2225	417	0.6663104	1
4874	417	0.6663104	
40/4	11	1 0.0000	

5061	417	0.6663104	;
1468	417	0.6663104	
264	417	0.6663104	
3962	417	0.6663104	
868	414	0.6636651	
5182	414	0.6636651	:
1353	414	0.6636651	
2192	414	0.6636651	
3289	414	0.6636651	
4256	414	0.6636651	rpIP
3558	414	0.6636651	
2674	411	0.6609989	
3611	411	0.6609989	
	411	0.6609989	сусВ
5300 2769	411	0.6609989	
	408	0.6583116	
3960	408	0.6583116	
1203	408	0.6583116	rnpA
5569		0.6583116	sspB
4427	408	0.6583116	3300
1129	408		
1465	408	0.6583116	
1645	408	0.6583116	
1659	408	0.6583116	£
4764	405	0.6556029	fur
778	405	0.6556029	
474	405	0.6556029	
5404	405	0.6556029	
398	405	0.6556029	
2016	405	0.6556029	
1883	399	0.650121	
5144	399	0.650121	
2827	399	0.650121	
2107	399	0.650121	<u> </u>
5543	. 399	0.650121	
3674	399	0.650121	
4778	399	0.650121	
1358	399	0.650121	
2706	396	0.6473475	
1250	396	0.6473475	aprl
710	396	0.6473475	gloA2
3788	396	0.6473475	
42	396	0.6473475	
2375	396	0.6473475	
5195	396	0.6473475	
4405	396	0.6473475	
2605	396	0.6473475	
3904	396	0.6473475	
4471	396	0.6473475	
4249	393	0.6445519	rpsH
	393	0.6445519	1
5347	393	0.6445519	hpcD
4125	393	0.6445519	rpsl
4432	1 333	, 0.0170010	

		0.0445540	
3967	393	0.6445519	
2722	393	0.6445519	
5328	390	0.6417342	
4240	390	0.6417342	rpsK
4237	390	0.6417342	rplQ
4747	390	0.6417342	secG
1817	390	0.6417342	
3432	390	0.6417342	
3884	387	0.6388941	
3813	387	0.6388941	iscU
1581	387	0.6388941	sdhC
540	387	0.6388941	
3021	387	0.6388941	
4383	384	0.6360315	
4392	384	0.6360315	
2446	384	0.6360315	gcvH2
5566	. 384	0.6360315	
3869	384	0.6360315	
1160	384	0.6360315	
3906	384	0.6360315	
867	384	0.6360315	
4731	381	0.6331462	panD
1355	381	0.6331462	
3041	381	0.6331462	
5339	381	0.6331462	
880	381	0.6331462	
1095	381	0.6331462	
5561	381	0.6331462	atpl
591	381	0.6331462	
1518	381	0.6331462	
170	381	0.6331462	
4603	381	0.6331462	(
3123	378	0.6302381	
4424	378	0.6302381	
4586	378	0.6302381	
3178	378	0.6302381	
991	378	0.6302381	
4059	378	0.6302381	
4485	378	0.6302381	
5381	378	0.6302381	
908	375	0.6273069	
2490	375	0.6273069	
680	375	0.6273069	ļ
2753	375	0.6273069	1
1456	375	0.6273069	cheY
3012	375	0.6273069	
4076	375	0.6273069	
4315	375	0.6273069	mvaT
3439	372	0.6243525	folX
4268	372	0.6243525	rpsL
5333	372	0.6243525	<u> </u>
2898	369	0.6213746	<u> </u>

	260	0.6213746	 :
5533	369 i	0.6213746	
1541	369	0.6213746	rpiN
4253	369	0.6213746	- Ipiix
3833	369	0.6213746	
1149 i	369	0.6213746	rplL
4271	369		secE
4276	369	0.6213746	sdhD
1582	369	0.6213746	SUID
2166	366	0.6183732	
33	366	0.6183732	
1701	366	0.6183732	
1842	363	0.6153479	
1378	363	0.6153479	
3203	363	0.6153479	
1840	363	0.6153479	
3843	363	0.6153479	
1076	363	0.6153479	
630	363	0.6153479	
613	360	0.6122987	
2901	360	0.6122987	
2606	360	0.6122987	
4324	360	0.6122987	
2868	360	0.6122987	<u> </u>
1492	357	0.6092253	<u> </u>
4005	357	0.6092253	<u> </u>
2741	357	0.6092253	rplT
2666	357	0.6092253	
1426	357	0.6092253	
4241	357	0.6092253	rpsM
2960	357	0.6092253	pilZ
871	357	0.6092253	phhB
1995	357	0.6092253	
2667	354	0.6061275	
5303	354	0.6061275	
582	354	0.6061275	folB
1568	354	0.6061275	
2736	354	0.6061275	
563	354	0.6061275	-
1349	351	0.6030052	+
665	351	0.6030052	rplR
4247	351	0.6030052	- Ipin
320	351	0.6030052	rplS
3742	351	0.6030052	This
3835	351	0.6030052	
1228	351	0.6030052	-
2175	348	0.5998581	
729	348	0.5998581	
570	348	0.5998581	- resG
1720	348	0.5998581	pscG
4711	348	0.5998581	-
3684	348	0.5998581	
4702	348	0.5998581	1

3664	348		·
1917	348	0.0990001	
2190	345	0.5966861	
2762	345	0.5966861	
3688	345	0.5966861	
2780	345 :	0.5966861	
3046	345	0.5966861	
4739	345		
1398	342	0.5934889	
128	342	0.5934889	
4575	342	0.5934889	
2456	342	0.5934889	
2781	342	0.5934889	
2715	339	0.5902664	
5288	339	0.5902664	glnK
3809	339	0.5902664	fdx2
3822	339	0.5902664	
1055	339	0.5902664	
1722	339	0.5902664	pscl
3367	339	0.5902664	
565	339	0.5902664	· ·
2608	336	0.5870183	
1965	336	0.5870183	
644	336	0.5870183	
825	336 .	0.5870183	
1114	336	0.5870183	
5275	336	0.5870183	
5067	336	0.5870183	hisE
589	333	0.5837445	
4258	333	0.5837445	rplV
4990	333	0.5837445	
1323	333	0.5837445	
5406	333	0.5837445	
3979	333	0.5837445	
3140	330	0.5804447	
2405	330	0.5804447	
1540	330	0.5804447	
3275	330	0.5804447	
4698	330	0.5804447	
1702	330	0.5804447	
3040	330	0.5804447	
939	327	0.5771188	
1925	327	0.5771188	
1780	327	0.5771188	nirD
4577	327	0.5771188	
3533	327	0.5771188	
2694	327	0.5771188	
5240	327	0.5771188	trxA
617	327	0.5771188	
1533	327	0.5771188	<u> </u>
4164	327	0.5771188	
1882	324	0.5737665	<u> </u>

		0.5707005	
3351 i	324	0.5737665	
894	324	0.5737665	
3042	324	0.5737665	i
1362	324	0.5737665	
3812	324	0.5737665	iscA
802	324	0.5737665	
4853	324	0.5737665	fis
2384	324	0.5737665	
488	321	0.5703877	
1123	321	0.5703877	
1676	321	0.5703877	
1168	321	0.5703877	
5417	321	0.5703877	soxD
3502	318	0.566982	
1038	318	0.566982	
15	318	0.566982	
2422	315	0.5635494	
3854	315	0.5635494	
610	315	0.5635494	prtN
4252	315	0.5635494	rplX
2658	315	0.5635494	
1830	315	0.5635494	
4753	315	0.5635494	
922	315	0.5635494	
2759	315	0.5635494	
5227	315	0.5635494	
4264	312	0.5600895	rpsJ
3260	312	0.5600895	
4568	312	0.5600895	rpiU
742	309	0.5566022	· · · · · · · · · · · · · · · · · · ·
2937	309	0.5566022	
2646	309	0.5566022	nuoK
979	309	0.5566022	
4463	309	0.5566022	
4452	309	0.5566022	
2174	309	0.5566022	
	309	0.5566022	
1937 786	306	0.5530873	
	306	0.5530873	
3142	306	0.5530873	
4674	306	0.5530873	
3347		0.5530873	
2161	306	0.5530873	pchB
4230	306	0.5530873	Pond
2245	306	0.5530873	
4789	306	0.5530873	rpsN
4250	306		Ihala
2607	306	0.5530873	bolA
857	306	0.5530873	אוטנא
466	303	0.5495445	
3390	303	0.5495445	+
647	303	0.5495445	
3298	303	0.5495445	1

		0.5405445	him A
2738	303	0.5495445	himA
4354	303	0.5495445	
3278 :	300	0.5459736	
4261	300	0.5459736	rpiW
2029	300	0.5459736	
4141	300	0.5459736	
3202	300	0.5459736	
2799	300	0.5459736	
2460	297	0.5423744	
1929	297	0.5423744	
709	297	0.5423744	
4875	297	0.5423744	
1705	297	0.5423744	pcrG
3662	294	0.5387467	
4419	294	0.5387467	ftsL
4386	294	0.5387467	groES
3566	294	0.5387467	
1295	294	0.5387467	
490	294	0.5387467	
900	291	0.5350903	
4482	291	0.5350903	gatC
369	291	0.5350903	
4642	291	0.5350903	
3338	291	0.5350903	
4638	288	0.5314048	
2143	288	0.5314048	
983	288	0.5314048	
131	288	0.5314048	
3274	288	0.5314048	
980	285	0.5276901	
3634	285	0.5276901	
3161	285	0.5276901	himD
4298	285	0.5276901	
2183	285	0.5276901	
3998	282	0.523946	
3051	282	0.523946	1
124	282	0.523946	
2292	282	0.523946	
3940	282	0.523946	
4176	282	0.523946	ppiC2
2697	282	0.523946	
1641	279	0.5201722	
3033	279	0.5201722	
1988	279	0.5201722	pgqD
1996	279	0.5201722	ppiC1
2485	279	0.5201722	FP.U
4060	279	0.5201722	
2723	279	0.5201722	
4637	279	0.5201722	
4018	276	0.5163685	
	276	0.5163685	rpsT
4563	276	0.5163685	ipa1
909		J 0.0 100000	

	670	0.5163685	rpsS
4259	276	0.5163685	
68	276	0.5163685	 j
954	276		
1852	276	0.5163685	
1298	276	0.5163685	
5148	273	0.5125346	
734 '	273	0.5125346	
4466	273	0.5125346	
2487	273	0.5125346	[
818	273	0.5125346	
2182	270	0.5086704	
1447	270	0.5086704	fliQ
4033	270	0.5086704	
4741	270	0.5086704	rpsO
4870	267	0.5047755	
3413	267	0.5047755	
4254	267	0.5047755	rpsQ
874	267	0.5047755	
1963	267	0.5047755	
2805	264	0.5008497	
3601	264	0.5008497	
3085	264	0.5008497	
986	264	0.5008497	
	264	0.5008497	imm2
1151	261	0.4968928	
1508 712	258	0.4929045	
1968	258	0.4929045	
2663	258	0.4929045	
1719	258	0.4929045	pscF
5559	258	0.4929045	atpE
1233	258	0.4929045	
	258	0.4929045	
384	258	0.4929045	rpmA
4567	258	0.4929045	<u> </u>
2737	255	0.4888847	
635	255	0.4888847	grx
5129	255	0.4888847	
1394	255	0.4888847	<u> </u>
4611		0.4888847	
53	255 255	0.4888847	<u> </u>
2031		0.4888847	minE
3245	255	0.4848329	moaD
3917	252	0.4848329	opri
2853	252	9 0.4848329	
1063	252	0.4848329	rpsP
3745	252	0.4848329	fdx1
362	252	0.4848329	1 14/1
1006			
4944	249	0.4807491	
493	249	1 0.4807491	tatA
5068	249	0.4807491	- lain
	249	0.4807491	1
3632 4782	246	0.4766328	

2429	246	0.4766328	
1711	246	0.4766328	
2297	246	0.4766328	
738	246	0.4766328	
4134	243	0.472484	
4377	243	0.472484	
1431	243	0.472484	rsaL
4357	243	0.472484	
2149	243	0.472484	
1849	243	0.472484	
1869	240	0.4683022	
1564	240	0.4683022	
3334	240	0.4683022	
1743	240	0.4683022	
2621	237	0.4640873	
1592	237	0.4640873	
	237	0.4640873	rpmB
5316	237	0.4640873	acpP
2966	234	0.459839	
2845	234	0.459839	
3009		0.459839	
60	234	0.459839	
2703	234	0.455557	
505	231	0.45557	rpsR
4934	231	0.45557	Their
648	231	<u> </u>	
632	231	0.455557	
1404	228	0.451241 0.451241	
805	228	0.451241	
125	228	0.451241	
39	228	1	
2992	228	0.451241 0.451241	
4359	228	0.451241	
2021	225		<u> </u>
3530	222	0.4425063	
2453	222	0.4425063	<u> </u>
1855	222	0.4425063	ļ
3612	222	0.4425063	<u> </u>
3031	222	0.4425063	<u> </u>
4028	222	0.4425063	
3237	222	0.4425063	
2785	219	0.4380869	
3501	219	0.4380869	
2412	219	0.4380869	<u> </u>
2619	219	0.4380869	infA
4306	219	0.4380869	<u> </u>
4826	219	0.4380869	<u> </u>
38	216	0.4336324	
4737	216	0.4336324	<u> </u>
579	216	0.4336324	rpsU
717	213	0.4291427	
3049	213	0.4291427	rmf
5526	213	0.4291427	<u> </u>

	242	0.4291427	
5460	213	0.4291427	
200	213	0.4246174	
2763	210 210	0.4246174	
1548	210	0.4246174	
2170	210	0.4246174	
456		0.4246174	
4823	210	0.4246174	
109	210	0.4246174	
960	210	0.4246174	
2668	210	0.4246174	
. 1159	210	0.4246174	capB
3266	210		Сары
3451	210	0.4246174	
627	207	0.4200562	
5403	207	0.4200562	
4077	207	0.4200562	pscE
1718	204	0.4154588	pscc
4530	201	0.410825	
380	201	0.410825	
553	201	0.410825	-
3808	201	0.410825	
1936	201	0.410825	
4738	198	0.4061544	
1230	198	0.4061544	
3520	195	0.4014469	
3752	195	0.4014469	
5480	195	0.4014469	rom!
2742	195	0.4014469	rpml
2808	192	0.396702	C
4255	192	0.396702	rpmC
1747	189	0.3919195	csrA
905	186	0.3870991 0.3870991	CSIA
3371	186		! [
258	186	0.3870991 0.3870991	
2980	186		
4940	186	0.3870991	
284	183	0.3822405 0.3822405	rpmF
2970	183	0.3773433	ipiiii
1571	180	0.3773433	<u> </u>
3496	180		
1478	177	0.3724074	<u> </u>
5408	177	0.3724074	
3572	177	0.3724074 0.3724074	rpmD
4245	177	0.3724074	1 IDITIO
2186	171	0.3624178	
4537	171		-
2501	168	0.3573635	-
2883	168	0.3573635	PODE
1177	168	0.3573635	napE
5351	168	0.3573635	
5350	168	0.3573635	
2146	168	0.3573635	1

3719	162	0.3471344	: !
5482	162	0.3471344	<u> </u>
2311	159	0.341959	: !
567	159	0.341959	
161	153	0.3314847	<u> </u>
3600	153	0.3314847	
3990	153	0.3314847	
3370	147	0.3208437	
135	141	0.3100333	
5276	141	0.3100333	lppL
1664	141	0.3100333	
5570	135	0.2990509	rpmH
3144	120	0.2708239	
442	117	0.2650435	
4242	117	0.2650435	rpmJ
1632	90	0.210914	kdpF
1985	72	0.1726306	Appq
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| Figure 1997 Commission Protein_NameCommission Commission Protein_NameCommission Commission |--|
| DNA-directed RNA polymerase beta* chain |
| DNA-directed RNA polymerase beta chain |
| iDNA polymerase III, alpha chain |
| ribonucleoside reductase, large chain |
| valyl-tRNA synthetase |
| isoleucyl-tRNA synthetase |
| organic solvent tolerance protein OstA precursor |
| DNA gyrase subunit A |
| secretion protein SecA |
| alanyl-tRNA synthetase |
| leucyl-tRNA synthetase |
| aconitate hydratase 2 |
| DNA topoisomerase I |
| translation initiation factor IF-2 |
| cell division protein FtsK |
| DNA gyrase subunit B |
| Lon protease |
| probable outer membrane protein |
| DNA ligase |
| phenylalanyl-tRNA synthetase, beta subunit |
| probable chemotaxis sensor/effector fusion protein |
| topoisomerase IV subunit A |
| primosomal protein N' |
| hypothetical protein |
| hypothetical protein |
| elongation factor G |
| polyribonucleotide nucleotidyltransferase |
| glycyl-tRNA synthetase beta chain |
| DNA polymerase subunits gamma and tau |
| methionyl-tRNA synthetase |
| ATP-dependent DNA helicase Rep |
| hypothetical protein |
| cytochrome C-type biogenesis protein CcmF |
| probable chemotaxis transducer |
| threonyl-tRNA synthetase |
| probable heat shock protein (hsp90 family) |
| heat shock protein HtpG |
| probable acetyltransferase |
| topoisomerase IV subunit B |
| 1-deoxyxylulose-5-phosphate synthase |
| hypothetical protein |
| secretion protein SecD |
| heat shock protein HscA |
| probable binding protein component of ABC transporter |
| glucosaminefructose-6-phosphate aminotransferase |
| transport protein MsbA |
| GTP-binding protein LepA |
| probable acyl-CoA dehydrogenase |
| succinate dehydrogenase (A subunit) |
| Succinate deliverogenase (A subtrity |
| arginyl-tRNA synthetase probable sodium/proton antiporter |
| probable social improtori |

probable acetyltransferase
penicillin-binding protein 3
conserved hypothetical protein
probable oxidoreductase
acetolactate synthase large subunit
single-stranded-DNA-specific exonuclease RecJ
prolyl-tRNA synthetase
urease alpha subunit
type 4 fimbrial biogenesis protein PilB
30S ribosomal protein S1
glutaminyl-tRNA synthetase
glucose-6-phosphate isomerase
hypothetical protein
electron transfer flavoprotein-ubiquinone oxidoreductase
GroEL protein
CTP synthase
probable chemotaxis transducer
arylsulfatase
conserved hypothetical protein
GMP synthase
hypothetical protein
probable carbohydrate kinase
phosphoglycerate mutase
conserved hypothetical protein
chromosomal replication initiator protein DnaA
ATP synthase alpha chain
hypothetical protein
apolipoprotein N-acyltransferase
hypothetical protein
xylulose kinase
general secretion pathway protein E
sodium/proton antiporter NhaB
probable colicin-like toxin
methylmalonate-semialdehyde dehydrogenase
RNA polymerase sigma-54 factor
probable transporter
N utilization substance protein A
hypothetical protein
probable flavin-binding monooxygenase
conserved hypothetical protein
UDP-N-acetylmuramoylalanyl-D-glutamate-2, 6-diaminopimelate ligase
hypothetical protein
probable amidase
outer membrane protein OprM precursor
RND divalent metal cation efflux membrane fusion protein CzcB precursor
Glu-tRNA(Gln) amidotransferase subunit A
pyruvate kinase II
probable Mg transporter MgtE
Glu-tRNA(Gln) amidotransferase subunit B
UDP-N-acetylmuramatealanine ligase
lipoamide dehydrogenase-glc
probable transporter (membrane subunit)
probable deliberation (maintains en en en en en en en en en en en en en

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conserved hypothetical protein
probable outer membrane protein
probable ferredoxin
glutamine synthetase
probable type II secretion system protein
nitrite extrusion protein 2
probable amidase .
soluble pyridine nucleotide transhydrogenase
replicative DNA helicase
probable glyceraldehyde-3-phosphate dehydrogenase
probable glyceralderryde-o-priospriate derrydrogenide
cysteinyl-tRNA synthetase exodeoxyribonuclease VII large subunit
exodeoxyribonuclease virialige subdifit UDP-N-acetylmuramoylalanyl-D-glutamyl-2, 6-diaminopimelateD-alanyl-D-alanyl ligase
UDP-N-acetylmuramoylalariyi-D-giutariiyi-z, o-diariiriopiriotatu basha ahain
ATP synthase beta chain
signal recognition particle protein Ffh
adenylosuccinate lyase
signal recognition particle receptor FtsY
probable 2-isopropylmalate synthase
conserved hypothetical protein
hypothetical protein
hypothetical protein
probable dicarboxylate transporter
biotin carboxylase
tryptophanyl-tRNA synthetase
UDP-N-acetylmuramoylalanineD-glutamate ligase
NADH dehydrogenase I chain F
probable aldolase
hypothetical protein
two-component response regulator PilR
phosphoglucosamine mutase
aminopeptidase P
probable cytochrome P450
conserved hypothetical protein
secretion protein SecY
hypothetical protein
probable MFS transporter
hypothetical protein
probable MFS transporter
porin O precursor
B-band O-antigen polymerase
conserved hypothetical protein
probable LIDP-ducose/GDP-mannose dehydrogenase WbpA
probable binding protein component of ABC maltose/mannitol transporter
C4-dicarboxylate transport protein
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
TolB protein
hypothetical protein
adenylosuccinate synthetase
peptidyl-prolyl cis-trans isomerase SurA
enolase
Eliolase

hypothetical protein
glutamate-1-semialdehyde 2,1-aminomutase
seryl-tRNA synthetase
3-deoxy-D-manno-octulosonic-acid (KDO) transferase
hypothetical protein
3-oxoacyl-acyl carrier protein synthase II
glutamyl-tRNA reductase
UDP-N-acetylglucosamine 1-carboxyvinyltransferase
hypothetical protein
transcription termination factor Rho
cell division protein FtsA
hypothetical protein
conserved hypothetical protein
ribonucleoside reductase, small chain
probable glycosyl transferase WbpJ
hypothetical protein
aspartate kinase alpha and beta chain
O-antigen translocase
hypothetical protein
hypothetical protein
probable transporter (membrane subunit)
conserved hypothetical protein
probable MFS transporter
conserved hypothetical protein
probable hydrolase
hypothetical protein
GTP-binding protein Obg
probable FAD-dependent monooxygenase
hypothetical protein
phenazine biosynthesis protein PhzC
probable type II secretion system protein
probable MFS transporter
conserved hypothetical protein
nitrate transporter
probable cytochrome b
hypothetical protein
DNA/pantothenate metabolism flavoprotein
membrane protein OpdE
two-component sensor
probable acyl-CoA thiolase
8-amino-7-oxononanoate synthase
conserved hypothetical protein
cell division protein FtsW
hypothetical protein
probable FAD-dependent monooxygenase
conserved hypothetical protein
probable MFS transporter
probable acyl-CoA thiolase
hypothetical protein
1-deoxy-d-xylulose 5-phosphate reductoisomerase
methionine adenosyltransferase
cell division protein FtsZ

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hypothetical protein
probable pyridoxal-phosphate dependent enzyme
acetyl-CoA acetyltransferase
probable molybdopterin biosynthesis protein MoeB
conserved hypothetical protein
hypothetical protein
lalginate biosynthesis protein Alg44
laiginate biosynthesis protein Ag44
hypothetical protein
probable hydrolase
succinyl-CoA synthetase beta chain
hypothetical protein
probable ATP-binding component of ABC transporter
probable acyl-CoA dehydrogenase
phosphoglycerate kinase
hypothetical protein
hypothetical protein
probable RND efflux membrane fusion protein precursor
probable peptidic bond hydrolase
probable multidrug resistance efflux pump
succinyl-diaminopimelate desuccinylase
conserved hypothetical protein
probable acyl-CoA dehydrogenase
general secretion pathway protein L
probable permease of ABC transporter
erythronate-4-phosphate dehydrogenase
conserved hypothetical protein
hypothetical protein
probable acyl-CoA thiolase
conserved hypothetical protein
lipid A-disaccharide synthase
LPS biosynthesis protein WbpG
hypothetical protein
tRNA methyltransferase
probable acyl-CoA dehydrogenase
conserved hypothetical protein
conserved hypothetical protein
still frameshift type 4 fimbrial biogenesis protein PilC
cytochrome c oxidase, subunit II
conserved hypothetical protein
riboflavin-specific deaminase/reductase
ripotiavin-specific dearminase/reductase
probable glycosyltransferase WbpH
glycine cleavage system protein T2
muconate cycloisomerase I
UDP-glucose:(heptosyl) LPS alpha 1,3-glucosyltransferase WaaG
hypothetical protein
glutamate 5-kinase
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
aspartate semialdehyde dehydrogenase
rod shape-determining protein

alcohol dehydrogenase (Zn-dependent) conserved hypothetical protein hypothetical protein peptide chain release factor 2 hypothetical protein conserved hypothetical protein hypothetical protein conserved hypothetical protein hypothetical protein conserved hypothetical protein conserved hypothetical protein conserved hypothetical protein peptide chain release factor 1 phospho-N-acetylmuramoyi-pentapeptide-transferase peptide chain release factor 1 phospho-N-acetylmuramoyi-pentapeptide-transferase probable aminotransferase WbpE probable aminotransferase WbpE probable aminotransferase WbpE probable aminotransferase WbpE probable manscriptional regulator UDP-N-acetylglucosamine-N-acetylmuramyi-(pentapeptide) pyrophosphoryi-undecaprenol N-acetylglucosamine to uroporphyrinogen decarboxylase hypothetical protein hypothetical protein hypothetical protein hypothetical protein hypothetical protein probable protein probable aminotransferase I LipP-3-O-18-yndroxylauroyi glucosamine N-acytiransferase guinolinate synthetase A probable beryndroxylauroyi glucosamine N-acytiransferase guinolinate synthetase A probable secretion protein probable alcohol dehydrogenase (Zn-dependent) conserved hypothetical protein conserved hypothetical protein rod shape-determining protein byre from hypothetical protein hypothetical protein hypothetical protein laransiccation protein protein hypothetical protein	
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O6-methylguanine-DNA methyltransferase probable transcriptional regulator UDP-N-acetylglucosamine-N-acetylmuramyl-(pentapeptide) pyrophosphoryl-undecaprenol N-acetylglucosamine truroporphyrinogen decarboxylase hypothetical protein heptosyltransferase I conserved hypothetical protein fructose-1.6 bisphosphate aidolase type 4 fimbrial biogenesis protein PilM probable UDP-N-acetylglucosamine 2-epimerase Wbpl phosphoribosylaminoimidazole synthetase UDP-3-o-[3-hydroxylauroyl] glucosamine N-acyltransferase quinolinate synthetase A probable secretion protein probable alcohol dehydrogenase (Zn-dependent) conserved hypothetical protein datase outer membrane protein OprF precursor hypothetical protein acetylpolyamine aminohydrolase conserved hypothetical protein pro	probable aminotransferase WbpE
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lipoate synthase hypothetical protein

hypothetical protein

conserved hypothetical protein

probable transcriptional regulator

conserved hypothetical protein
conserved hypothetical protein
delta 2-isopentenylpyrophosphate transferase
octaprenyl-diphosphate synthase
hypothetical protein
hypothetical protein
probable enoyl-CoA hydratase/isomerase
Ithiamine monophosphate kinase
hypothetical protein
hypothetical protein
hypothetical protein
probable serine/threonine dehydratase, degradative
pseudouridine synthase
conserved hypothetical protein
hypothetical protein
ribosomal large subunit pseudouridine synthase C
Indosomal large subulit pseudoundine synthase o
probable transcriptional regulator
hypothetical protein probable transmembrane sensor
hypothetical protein
probable transcriptional regulator
probable transcriptional regulator
glutathione synthetase
hypothetical protein
probable adhesion protein acetyl-coenzyme A carboxylase carboxyl transferase (alpha subunit)
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probable transcriptional regulator probable NAD-dependent epimerase/dehydratase WbpK
probable oxidoreductase WpbB
probable transmembrane sensor
hypothetical protein glycyl-tRNA synthetase alpha chain
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probable lipase
LytB protein
conserved hypothetical protein
probable hydrolase
ribose-phosphate pyrophosphokinase
hypothetical protein
conserved hypothetical protein
porphobilinogen deaminase
probable transcriptional regulator
probable lauroyl acyltransferase
transcriptional regulator PtxR
probable transcriptional regulator
hypothetical protein
malonyl-CoA-[acyl-carrier-protein] transacylase
riboflavin kinase/FAD synthase
conserved hypothetical protein
conserved hypothetical protein
probable phosphatidate cytidylyltransferase
hypothetical protein
carbamate kinase

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hypothetical protein
probable transcriptional regulator
catechol 1,2-dioxygenase
D-alanyl-D-alanine-endopeptidase
probable transcriptional regulator
hypothetical protein
probable epimerase
lipase LipC
probable transcriptional regulator
electron transfer flavoprotein alpha-subunit
FdhE protein
hypothetical protein
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conserved hypothetical protein
probable ATP-binding component of ABC transporter
probable cytochrome c
probable transcriptional regulator
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probable permease of ABC transporter
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GTP-binding protein Era
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probable cytochrome c oxidase assembly factor
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probable short chain dehydrogenase
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UDP-3-O-acyl-N-acetylglucosamine deacetylase
probable transcriptional regulator
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cytochrome o ubiquinol oxidase protein CyoE
probable 3-hydroxyisobutyrate dehydrogenase
probable transcriptional regulator
4-hydroxybenzoate-octaprenyl transferase
probable chemotaxis protein
iconserved hypothetical protein
probable 2-OH-lauroyitransferase
probable transcriptional regulator
succinyl-CoA synthetase alpha chain
conserved hypothetical protein
geranyltransfransferase
hypothetical protein
ribosomal protein L11 methyltransferase
olucose-1-phosphate thymidylyltransferase
conserved hypothetical protein
hypothetical protein
dihydrodipicolinate synthase
heat shock protein HtpX
methyltransferase PilK
probable transcriptional regulator
conserved hypothetical protein
hypothetical protein
chromosome partitioning protein Spo0J
hypothetical protein
acetyl-CoA carboxylase beta subunit
elongation factor Ts
cell division protein ZipA
ATP synthase A chain
outer membrane protein PopN
lipase modulator protein
hypothetical protein
probable transcriptional regulator
conserved hypothetical protein
hypothetical protein
cell division protein FtsQ
malonate decarboxylase beta subunit
ATP synthase gamma chain
probable hydrolase
hypothetical protein
probable short-chain dehydrogenase
spermidine synthase
probable ATP-binding component of ABC transporter
hypothetical protein
hypothetical protein
probable ATP-binding component of ABC transporter
hypothetical protein

probable transcriptional regulator
5,10-methylene-tetrahydrofolate dehydrogenase / cyclohydrolase
sigma factor RpoH
signal peptidase I
hypothetical protein
formyltetrahydrofolate deformylase
dihydropteroate synthase
conserved hypothetical protein
probable potassium channel
isopentenyl monophosphate kinase
Isopentenyi monophosphate kinase
hypothetical protein
hypothetical protein
nicotinate-nucleotide pyrophosphorylase
conserved hypothetical protein
hypothetical protein
2-dehydro-3-deoxyphosphooctonate aldolase
probable transmembrane sensor
urease accessory protein
flagellar synthesis regulator FleN
probable ATP-binding component of ABC transporter
probable phenazine biosynthesis protein
ATP-binding component of ABC phosphonate transporter
probable ATP-binding component of ABC transporter
probable permease of ABC transporter
probable short-chain dehydrogenase
diaminopimelate epimerase
probable two-component response regulator
conserved hypothetical protein
NH3-dependent NAD synthetase
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probable biotin synthesis protein BioC
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type 4 fimbrial biogenesis protein PilW
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50S ribosomal protein L2
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probable oxidoreductase
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probable permease of ABC transporter
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dihydrodipicolinate reductase
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hypothetical protein WaaP
lipopolysaccharide core biosynthesis protein WaaP
tryptophan synthase alpha chain
probable ATP-binding component of ABC transporter
hypothetical protein
probable permease of ABC-2 transporter
probable transcriptional regulator
conserved hypothetical protein
prolipoprotein diacylglyceryl transferase
3-methyl-2-oxobutanoate hydroxymethyltransferase
glutamate racemase
conserved hypothetical protein
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probable enoyl-CoA hydratase/isomerase
probable transcriptional regulator
conserved hypothetical protein
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translocation protein in type III secretion
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probable pili assembly chaperone
probable transcriptional regulator
probable plasmid partitioning protein
probable permease of ABC transporter
conserved hypothetical protein
methionine aminopeptidase
conserved hypothetical protein
hypothetical protein
hypothetical protein
probable transcriptional regulator
probable permease of ABC-2 transporter
probable NAD(P)H dehydrogenase
conserved hypothetical protein
hypothetical protein
UDP-N-acetylglucosamine acyltransferase
ferredoxinNADP+ reductase
probable permease of ABC transporter
conserved hypothetical protein
probable enoyl-CoA hydratase/isomerase
Inclyamine transport protein PotC
ubiquinone biosynthesis methyltransferase UbiE
hypothetical protein
transcriptional regulator PrtR
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probable transcriptional regulator
conserved hypothetical protein
probable exopolysaccharide transporter
probable ATP-binding component of ABC transporter
hypothetical protein
probable short-chain dehydrogenase
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3-deoxy-manno-octulosonate cytidylyltransferase
probable transporter
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cis-1,2-dihydroxycyclohexa-3,4-diene carboxylate dehydrogenase
probable enoyl-CoA hydratase/isomerase
molybdopterin biosynthesis MoeB protein
probable short-chain dehydrogenase
conserved hypothetical protein
heme exporter protein CcmC
hypothetical protein
tRNA (guanine-N1)-methyltransferase
type 4 fimbrial biogenesis protein PilF
imidazoleglycerol-phosphate synthase, cyclase subunit
conserved hypothetical protein
triosephosphate isomerase
uroporphyrinogen-III synthetase
undecaprenyl pyrophosphate synthetase
hypothetical protein
probable cobalamin biosynthetic protein
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probable short-chain dehydrogenase
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electron transfer flavoprotein beta-subunit
conserved hypothetical protein
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3-oxoacyl-[acyl-carrier-protein] reductase
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probable pili assembly chaperone
DNA polymerase III, epsilon chain
30S ribosomal protein S2
hypothetical protein
hypothetical protein
probable nucleoside phosphorylase

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uridylate kinase
hypothetical protein
probable permease of ABC transporter
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itranscriptional regulator RhIR
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probable ATP-binding component of ABC transporter
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probable biotin biosynthesis protein bioH
probable permease of ABC transporter
hypothetical protein
conserved hypothetical protein
ribonuclease PH
probable glutamine amidotransferase
conserved hypothetical protein
probable transcriptional regulator
conserved hypothetical protein
probable transcriptional regulator
DNA-specific endonuclease I
probable transcriptional regulator
hypothetical protein
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probable pili assembly chaperone
probable two-component response regulator
phosphoribosylaminoimidazole-succinocarboxamide synthase
succinate dehydrogenase (B subunit)
hypothetical protein
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probable ATP-binding component of ABC transporter
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hypothetical protein
probable transcriptional regulator
3-demethylubiquinone-9 3-methyltransferase
probable hydrolase
orotidine 5'-phosphate decarboxylase
hypothetical protein
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50S ribosomal protein L1
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probable permease of ABC transporter

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probable acetyltransferase
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TolQ protein
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probable pseudouridylate synthase
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two-component response regulator
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30S ribosomal protein S3
hypothetical protein
probable transcriptional regulator
dethiobiotin synthase
molybdenum transport protein ModB
transcriptional regulator Dnr
hypothetical protein
probable ATP-binding component of ABC transporter
leucyl/phenylalanyl-tRNA-protein transferase
conserved hypothetical protein
NADH dehydrogenase I chain B
probable two-component response regulator
hypothetical protein
probable transcriptional regulator
Na+-translocating NADH:uniquinone oxidoreductase subunit Nqr4
ribonuclease T
hypothetical protein
conserved hypothetical protein
DNA repair protein RadC
ribulose-phosphate 3-epimerase
hypothetical protein
hypothetical protein
heme exporter protein CcmB
hypothetical protein
urease accessory protein UreF
ribose 5-phosphate isomerase
phosphoribosylaminoimidazole synthetase
probable transcriptional regulator
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conserved hypothetical protein
probable acetyltransferase
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2-keto-3-deoxy-6-phosphogluconate aldolase
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pyridoxine 5'-phosphate oxidase
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probable carboxylesterase
pyoverdine biosynthesis protein PvcD
probable transcriptional regulator
probable carbonic anhydrase
conserved hypothetical protein
probable pyridoxamine 5'-phosphate oxidase
probable pyridoxamine 5'-phosphate oxidase
hypothetical protein
probable glutathione S-transferase
hypothetical protein
transcriptional regulator Vfr
hypothetical protein
orotate phosphoribosyltransferase
glutamine amidotransferase
hypothetical protein
hypothetical protein
maleylacetoacetate isomerase
probable radical activating enzyme
hypothetical protein
uracil phosphoribosyltransferase
hypothetical protein
endonuclease III
probable transcriptional regulator
probable antioxidant protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
probable tolQ-type transport protein
pseudouridine synthase RluA
conserved hypothetical protein
50S ribosomal protein L3
conserved hypothetical protein
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probable two-component response regulator
thymidylate kinase
conserved hypothetical protein
conserved hypothetical protein
probable aromatic acid decarboxylase

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hypothetical protein
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periplasmic chaperone LolA
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cell division protein FtsJ
hypothetical protein
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30S ribosomal protein S4
homoserine kinase
hypothetical protein
probable lipoprotein localization protein LolB
stringent starvation protein A
hypothetical protein
GTP cyclohydrolase II
hypothetical protein
heme acquisition protein HasAp
probable transcriptional regulator
probable peptide chain release factor
probable ribosomal protein L25
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conserved hypothetical protein
guanylate kinase
glutamine amidotransferase
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autoinducer synthesis protein Lasl
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cytochrome c-type protein NapC
conserved hypothetical protein
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hypothetical protein
probable DNA invertase
probable acetyltransferase WbpD
hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
ribosomal protein alanine acetyltransferase
probable transcriptional regulator
hypothetical protein
conserved hypothetical protein ,
conserved hypothetical protein
translation elongation factor P
conserved hypothetical protein
hypothetical protein
transcriptional regulator NfxB
probable transcriptional regulator
probable protease
alkyl hydroperoxide reductase subunit C
peptidyl-prolyl cis-trans isomerase A
hypothetical protein
hypothetical protein
hypothetical protein
GTP cyclohydrolase I precursor
probable transcriptional regulator
heat shock protein GrpE
CDP-diacylglycerolglycerol-3-phosphate 3-phosphatidyltransferase
conserved hypothetical protein
conserved hypothetical protein
Conserved hypothetical protein

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ribosome recycling factor
conserved hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
probable transcriptional regulator
conserved hypothetical protein
hypothetical protein
translation initiation factor IF-3
potassium-transporting ATPase, C chain
probable transcriptional regulator
conserved hypothetical protein
conserved hypothetical protein
adenine phosphoribosyltransferase
conserved hypothetical protein
dTDP-4-dehydrorhamnose 3,5-epimerase
hypothetical protein
probable sigma-70 factor, ECF subfamily
GTP cyclohydrolase I precursor
hypothetical protein
cytochrome C biogenesis protein CcmG
conserved hypothetical protein
50S ribosomal protein L5
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
ATP synthase delta chain
NosL protein
conserved hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
50S ribosomal protein L6
conserved hypothetical protein
conserved hypothetical protein
transcription antitermination protein NusG
hypothetical protein
hypothetical protein
conserved hypothetical protein
lactoyiglutathione lyase
outer membrane lipoprotein OmlA
hypothetical protein
inorganic pyrophosphatase
probable sigma-70 factor, ECF subfamily
conserved hypothetical protein
conserved hypothetical protein
hypothetical protein
16S rRNA processing protein
hypothetical protein
hypothetical protein
heme d1 biosynthesis protein NirL
hypothetical protein
hypothetical protein

general secretion pathway protein M
hypothetical protein
hypothetical protein
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
heat shock protein HscB
hypothetical protein
hypothetical protein
general secretion pathway protein H
conserved hypothetical protein
shikimate kinase
hypothetical protein
conserved hypothetical protein
phosphatidylglycerophosphatase A
beta-hydroxydecanoyl-ACP dehydrase
conserved hypothetical protein
transcriptional regulator PyrR
conserved hypothetical protein
spermidine acetyltransferase
prolipoprotein signal peptidase
hypothetical protein
conserved hypothetical protein
probable transcriptional regulator
conserved hypothetical protein
probable sigma-70 factor, ECF subfamily
conserved hypothetical protein
hypothetical protein
hypothetical protein
probable outer membrane protein precursor
probable outer membrane protein
hypothetical protein
transcription elongation factor GreB
dihydrofolate reductase
hypothetical protein
hypothetical protein
50S ribosomal protein L10
30S ribosomal protein S5
hypothetical protein
hypothetical protein
hypothetical protein
NADH dehydrogenase I chain J
hypothetical protein
hypothetical protein
hypothetical protein
single-stranded DNA-binding protein
hypothetical protein
secretion protein SecB
conserved hypothetical protein
cytochrome c-type protein NapB precursor
ferredoxin protein NapF
probable methyltransferase

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his protein
probable phenazine biosynthesis protein
probable phenazine biosynthesis protein
probable phenazine biosynthesis protein
hypothetical protein
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conserved hypothetical protein
toluate 1,2-dioxygenase beta subunit
2-amino-4-hydroxy-6-hydroxymethyldihydropteridine pyrophosphokinase
hypothetical protein
peptidyl-prolyl cis-trans isomerase SlyD
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molybdopterin biosynthetic protein C
conserved hypothetical protein
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NusB protein
phosphopantetheine adenylyltransferase
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
hypothetical protein
probable purine-binding chemotaxis protein
hypothetical protein
hypothetical protein
hypothetical protein
6,7-dimethyl-8-ribityllumazine synthase
hypothetical protein
conserved hypothetical protein
translocation protein in type III secretion
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein bacterioferritin comigratory protein
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conserved hypothetical protein
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ATP synthase B chain
30S ribosomal protein S7
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biotin carboxyl carrier protein (BCCP)
probable dna-binding stress protein
hypothetical protein
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cytochrome C-type biogenesis protein CcmH
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nitrogen regulatory IIA protein
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hypothetical protein conserved hypothetical protein
phosphotyrosine protein phosphatase
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osmotically inducible protein OsmC
deoxyuridine 5'-triphosphate nucleotidohydrolase
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molybdopterin converting factor, large subunit
conserved hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
probable type II secretion system protein
type 4 fimbrial precursor PilA
probable transcriptional regulator
hypothetical protein
hypothetical protein
3-dehydroguinate dehydratase
ribonuclease H
hypothetical protein
hypothetical protein
probable peptide deformylase
probable transcriptional regulator

flagellar protein FliJ
TolR protein
conserved hypothetical protein
(3R)-hydroxymyristoyl-[acyl carrier protein] dehydratase
hypothetical protein
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
probable transcriptional regulator
conserved hypothetical protein
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hypothetical protein exoenzyme S synthesis protein C precursor
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hypothetical protein
hypothetical protein
50S ribosomal protein L15
hypothetical protein
conserved hypothetical protein
hypothetical protein
conserved hypothetical protein
conserved hypothetical protein
hypothetical protein
probable type II secretion system protein
helix destabilizing protein of bacteriophage Pf1
hypothetical protein
nucleoside diphosphate kinase
50S ribosomal protein L11
hypothetical protein
hypothetical protein
50S ribosomal protein L13
hypothetical protein
hypothetical protein
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conserved hypothetical protein
probable transcriptional regulator
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probable type II secretion system protein
hypothetical protein
ATP synthase epsilon chain
hypothetical protein
conserved hypothetical protein
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30S ribosomal protein S6
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50S ribosomal protein L16
hypothetical protein
probable type II secretion system protein
hypothetical protein
cytochrome c5
hypothetical protein
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ribonuclease P protein component
stringent starvation protein B
probable fosfomycin resistance protein
hypothetical protein
hypothetical protein
hypothetical protein
ferric uptake regulation protein
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hypothetical protein
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probable transcriptional regulator
probable NADH-ubiquinone/plastoquinone oxidoreductase
hypothetical protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
hypothetical protein
probable transcriptional regulator
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hypothetical protein
alkaline proteinase inhibitor Apri
lactoylglutathione lyase
hypothetical protein
hypothetical protein
hypothetical protein
probable heat shock protein
hypothetical protein
conserved hypothetical protein
hypothetical protein
hypothetical protein
30S ribosomal protein S8
hypothetical protein
5-carboxymethyl-2-hydroxymuconate isomerase
30S ribosomal protein S9
305 fibosofilal protein 39

hypothetical protein	
hypothetical protein	
probable cytochrome c(mono-heme type)	
30S ribosomal protein \$11	
50S ribosomal protein L17	·
secretion protein SecG	
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hypothetical protein	
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probable iron-binding protein IscU	
succinate dehydrogenase (C subunit)	
hypothetical protein	The second secon
Inypothetical protein	
hypothetical protein	
conserved hypothetical protein	
conserved hypothetical protein	
glycine cleavage system protein H2	
hypothetical protein	
aspartate 1-decarboxylase precursor	
hypothetical protein	
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conserved hypothetical protein	
probable ring-cleaving dioxygenase	
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ATP synthase protein I	
conserved hypothetical protein	
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conserved hypothetical protein	
hypothetical protein	
hypothetical protein	
conserved hypothetical protein	
probable type II secretion system protein	
hypothetical protein	
two-component response regulator CheY	
hypothetical protein	
hypothetical protein	
transcriptional regulator MvaT, P16 subunit	
d-erythro-7,8-dihydroneopterin triphosphate	epimerase
30S ribosomal protein S12	
conserved hypothetical protein	
hypothetical protein	

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50S ribosomal protein L22
SMR multidrug efflux transporter
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probable transporter
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probable iron-binding protein IscA
hypothetical protein
DNA-binding protein Fis
hypothetical protein
conserved hypothetical protein
hypothetical protein
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sarcosine oxidase delta subunit
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transcriptional regulator PrtN
50S ribosomal protein L24
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50S ribosomal protein L21
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salicylate biosynthesis protein PchB
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conserved hypothetical protein
30S ribosomal protein S14
conserved hypothetical protein
Teambagono protein RolA
morphogene protein BolA
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integration host factor, alpha subunit
conserved hypothetical protein
hypothetical protein
50S ribosomal protein L23
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conserved hypothetical protein
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regulator in type III secretion
hypothetical protein
cell division protein FtsL
GroES protein
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conserved hypothetical protein
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Glu-tRNA(Gln) amidotransferase subunit C
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conserved hypothetical protein
integration host factor beta subunit
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probable DNA binding protein
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pyrrologuinoline quinone biosynthesis protein D
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30S ribosomal protein S19
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translocation protein TatA
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hypothetical protein of bacteriophage Pf1

ribosome modulation factor

hypothetical protein

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hypothetical protein
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carbon storage regulator
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50S ribosomal protein L32
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50S ribosomal protein L30
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periplasmic nitrate reductase protein NapE
rubredoxin
rubredoxin
conserved hypothetical protein

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50S ribosomal protein L36	
KdpF protein	
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031H10	21073	PAK
031H11	395319	PAK
032A01	3743984	PAK
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032B09	3971396	PAK
032B10	2101615	PAK
032B11	3848049	PAK
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032C03	2734352	PAK
032C04	5192269	PAK

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032C06	222082	PAK
032C07	5959665	PAK
032C08	960638	PAK
032C09	3788806	PAK
032C10	133768	PAK
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032C12	6246275	PAK
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032D02	824017	PAK
032D03	·· 703212	PAK
032D05	4617899	PAK
032D06	3161119	PAK
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032D08	5819393	PAK
032D10	944284	PAK
032D11	515164	PAK
032E01	2296065	PAK
032E03	1589174	PAK
· 032E04	3496720	PAK
032E05	4703559	PAK
032E06	3429859	PAK
032E07	1815893	PAK
032E08	4512079	PAK
032E09	5800124	PAK
032E10	1282182	PAK
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032G07	1034469	PAK
032G08	5523553	PAK
032G09	1082517	PAK
032G10	902337	PAK
032G11	2285758	PAK
032H01	4432184	PAK
032H02	312089	PAK
032H03	3157954	PAK
032H04	592072	PAK
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032H05 3584145 PAK 032H06 5259025 PAK 032H07 5040084 PAK 032H08 5776175 PAK 032H09 1470035 PAK 032H10 4999577 PAK 032H11 395319 PAK 033A02 5903292 PAK 033A04 3068005 PAK 033A05 2021360 PAK 033A06 4343557 PAK 033A07 4457135 PAK 033A09 1703596 PAK 033A11 193593 PAK 033B01 5215520 PAK 033B02 735223 PAK 033B03 280214 PAK 033B03 280214 PAK 033B06 5734271 PAK 033B07 464561 PAK 033B08 4158275 PAK 033B09 6076677 PAK 033B11 5139025 PAK	/:	00044451	DA14
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061E12	4044343	PAK pili-
061F01	3301676	PAK pili-
061F01	5828638	PAK pili-
061F03	5634333	PAK pili-
061F03	5318976	PAK pili-
061F05	3420298	PAK pili-
061F05 061F06	6028099	PAK pili-
061F09	2874916	PAK pili-
	1702230	PAK pili-
061F10		PAK pili-
061F11	164740	
061F12	4169592	PAK pili-
061G05	2126206	PAK pili-
061G07	815297	PAK pili-
061G08	6260187	PAK pili-

061G09 1347823 PAK pili- 061G10 3775399 PAK pili- 061G11 4218405 PAK pili- 061G12 1166408 PAK pili- 061H01 5609073 PAK pili- 061H02 4186785 PAK pili- 061H03 3069909 PAK pili- 061H04 6121348 PAK pili- 061H05 2909905 PAK pili- 061H06 790965 PAK pili- 061H07 2061539 PAK pili- 061H08 2874916 PAK pili- 061H09 245693 PAK pili- 061H01 5207481 PAK pili- 061H01 5207481 PAK pili- 062A02 2186046 PAK pili- 062A01 522496 PAK pili- 062A02 2186046 PAK pili- 062A03 881650 PAK pili- 062A04 108711 PAK pili- 062A05 4573163 PAK pili- 062A06 4592778 </th <th></th> <th>· · · · · · · · · · · · · · · · · · ·</th> <th></th>		· · · · · · · · · · · · · · · · · · ·	
061G11 4218405 PAK pili- 061G12 1166408 PAK pili- 061H01 5609073 PAK pili- 061H02 4186785 PAK pili- 061H03 3069909 PAK pili- 061H04 6121348 PAK pili- 061H05 2909905 PAK pili- 061H06 790965 PAK pili- 061H07 2061539 PAK pili- 061H08 2874916 PAK pili- 061H09 245693 PAK pili- 061H01 5207481 PAK pili- 061H01 5207481 PAK pili- 062A01 522496 PAK pili- 062A02 2186046 PAK pili- 062A03 881650 PAK pili- 062A04 108711 PAK pili- 062A05 4573163 PAK pili- 062A06 4592778 PAK pili- 062A07 2767284 PAK pili- 062A08 245488 PAK pili- 062A01 4883451 <td>061G09</td> <td>1347823</td> <td>PAK pili-</td>	061G09	1347823	PAK pili-
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061H05 2909905 PAK pili- 061H06 790965 PAK pili- 061H07 2061539 PAK pili- 061H08 2874916 PAK pili- 061H09 245693 PAK pili- 061H10 5207481 PAK pili- 061H11 395318 PAK pili- 062A01 522496 PAK pili- 062A02 2186046 PAK pili- 062A03 881650 PAK pili- 062A04 108711 PAK pili- 062A05 4573163 PAK pili- 062A06 4592778 PAK pili- 062A07 2767284 PAK pili- 062A08 245488 PAK pili- 062A09 245488 PAK pili- 062A01 4883451 PAK pili- 062B01 5814642 PAK pili- 062B01 5814642 PAK pili- 062B02 972216 PAK pili- 062B03 2482611 PAK pili- 062B04 3763613	061H03	3069909	
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061H08 2874916 PAK pili- 061H09 245693 PAK pili- 061H10 5207481 PAK pili- 061H11 395318 PAK pili- 062A01 522496 PAK pili- 062A02 2186046 PAK pili- 062A03 881650 PAK pili- 062A04 108711 PAK pili- 062A05 4573163 PAK pili- 062A06 4592778 PAK pili- 062A07 2767284 PAK pili- 062A08 245488 PAK pili- 062A09 245488 PAK pili- 062A09 245488 PAK pili- 062A01 4883451 PAK pili- 062A02 245488 PAK pili- 062B01 5814642 PAK pili- 062B02 972216 PAK pili- 062B03 2482611 PAK pili- 062B04 3763613 PAK pili- 062B05 3363603 PAK pili- 062B09 3363603	061H06	790965	
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061H10 5207481 PAK pili- 061H11 395318 PAK pili- 062A01 522496 PAK pili- 062A02 2186046 PAK pili- 062A03 881650 PAK pili- 062A04 108711 PAK pili- 062A05 4573163 PAK pili- 062A06 4592778 PAK pili- 062A07 2767284 PAK pili- 062A08 245488 PAK pili- 062A08 245488 PAK pili- 062A09 245488 PAK pili- 062A01 4883451 PAK pili- 062A11 4883451 PAK pili- 062B01 5814642 PAK pili- 062B02 972216 PAK pili- 062B03 2482611 PAK pili- 062B04 3763613 PAK pili- 062B07 6163753 PAK pili- 062B08 4880267 PAK pili- 062B10 202392 PAK pili- 062B11 245488	061H08	2874916	PAK pili-
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062A01 522496 PAK pili- 062A02 2186046 PAK pili- 062A03 881650 PAK pili- 062A04 108711 PAK pili- 062A05 4573163 PAK pili- 062A06 4592778 PAK pili- 062A07 2767284 PAK pili- 062A08 245488 PAK pili- 062A09 245488 PAK pili- 062A01 4883451 PAK pili- 062A11 4883451 PAK pili- 062B01 5814642 PAK pili- 062B02 972216 PAK pili- 062B03 2482611 PAK pili- 062B03 2482611 PAK pili- 062B04 3763613 PAK pili- 062B05 6163753 PAK pili- 062B06 4880267 PAK pili- 062B09 3363603 PAK pili- 062B10 202392 PAK pili- 062B1 202392 PAK pili- 062C01 2796578	061H10	5207481	
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062A03 881650 PAK pili- 062A04 108711 PAK pili- 062A05 4573163 PAK pili- 062A06 4592778 PAK pili- 062A07 2767284 PAK pili- 062A08 245488 PAK pili- 062A09 245488 PAK pili- 062A09 245488 PAK pili- 062A09 245488 PAK pili- 062A09 245488 PAK pili- 062A11 4883451 PAK pili- 062B01 5814642 PAK pili- 062B02 972216 PAK pili- 062B03 2482611 PAK pili- 062B04 3763613 PAK pili- 062B07 6163753 PAK pili- 062B08 4880267 PAK pili- 062B09 3363603 PAK pili- 062B10 202392 PAK pili- 062B11 245488 PAK pili- 062C02 1421710 PAK pili- 062C03 6193624	062A01	522496	PAK pili-
062A04 108711 PAK pili- 062A05 4573163 PAK pili- 062A06 4592778 PAK pili- 062A07 2767284 PAK pili- 062A08 245488 PAK pili- 062A09 245488 PAK pili- 062A09 245488 PAK pili- 062A09 245488 PAK pili- 062A11 4883451 PAK pili- 062B01 5814642 PAK pili- 062B02 972216 PAK pili- 062B03 2482611 PAK pili- 062B04 3763613 PAK pili- 062B05 972216 PAK pili- 062B06 4880267 PAK pili- 062B07 6163753 PAK pili- 062B08 4880267 PAK pili- 062B09 3363603 PAK pili- 062B10 202392 PAK pili- 062B11 245488 PAK pili- 062C01 2796578 PAK pili- 062C02 1421710	062A02	2186046	
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062A06 4592778 PAK pili- 062A07 2767284 PAK pili- 062A08 245488 PAK pili- 062A09 245488 PAK pili- 062A01 4883451 PAK pili- 062A12 245488 PAK pili- 062B01 5814642 PAK pili- 062B02 972216 PAK pili- 062B03 2482611 PAK pili- 062B03 2482611 PAK pili- 062B04 3763613 PAK pili- 062B07 6163753 PAK pili- 062B08 4880267 PAK pili- 062B09 3363603 PAK pili- 062B10 202392 PAK pili- 062B11 245488 PAK pili- 062C01 2796578 PAK pili- 062C02 1421710 PAK pili- 062C03 6193624 PAK pili- 062C04 4335461 PAK pili- 062C05 5582809 PAK pili- 062C06 1887384 <td>062A04</td> <td>108711</td> <td>PAK pili-</td>	062A04	108711	PAK pili-
062A07 2767284 PAK pili- 062A08 245488 PAK pili- 062A09 245488 PAK pili- 062A11 4883451 PAK pili- 062A12 245488 PAK pili- 062B01 5814642 PAK pili- 062B02 972216 PAK pili- 062B03 2482611 PAK pili- 062B04 3763613 PAK pili- 062B07 6163753 PAK pili- 062B08 4880267 PAK pili- 062B09 3363603 PAK pili- 062B10 202392 PAK pili- 062B11 245488 PAK pili- 062C01 2796578 PAK pili- 062C02 1421710 PAK pili- 062C03 6193624 PAK pili- 062C04 4335461 PAK pili- 062C05 5582809 PAK pili- 062C06 1887384 PAK pili- 062C07 2674834 PAK pili- 062C10 6126368 <td>062A05</td> <td>4573163</td> <td>PAK pili-</td>	062A05	4573163	PAK pili-
062A08 245488 PAK pili- 062A09 245488 PAK pili- 062A11 4883451 PAK pili- 062A12 245488 PAK pili- 062B01 5814642 PAK pili- 062B02 972216 PAK pili- 062B03 2482611 PAK pili- 062B04 3763613 PAK pili- 062B07 6163753 PAK pili- 062B08 4880267 PAK pili- 062B09 3363603 PAK pili- 062B10 202392 PAK pili- 062B11 245488 PAK pili- 062C01 2796578 PAK pili- 062C02 1421710 PAK pili- 062C03 6193624 PAK pili- 062C04 4335461 PAK pili- 062C05 5582809 PAK pili- 062C06 1887384 PAK pili- 062C07 2674834 PAK pili- 062C10 6126368 PAK pili- 062C11 6126368 <td>062A06</td> <td>4592778</td> <td>PAK pili-</td>	062A06	4592778	PAK pili-
062A09 245488 PAK pili- 062A11 4883451 PAK pili- 062A12 245488 PAK pili- 062B01 5814642 PAK pili- 062B02 972216 PAK pili- 062B03 2482611 PAK pili- 062B04 3763613 PAK pili- 062B07 6163753 PAK pili- 062B08 4880267 PAK pili- 062B09 3363603 PAK pili- 062B10 202392 PAK pili- 062B11 245488 PAK pili- 062C01 2796578 PAK pili- 062C02 1421710 PAK pili- 062C03 6193624 PAK pili- 062C04 4335461 PAK pili- 062C05 5582809 PAK pili- 062C06 1887384 PAK pili- 062C07 2674834 PAK pili- 062C10 6126368 PAK pili- 062C11 6126368 PAK pili- 062D01 3063043 </td <td>062A07</td> <td>2767284</td> <td>PAK pili-</td>	062A07	2767284	PAK pili-
062A11 4883451 PAK pili- 062A12 245488 PAK pili- 062B01 5814642 PAK pili- 062B02 972216 PAK pili- 062B03 2482611 PAK pili- 062B04 3763613 PAK pili- 062B07 6163753 PAK pili- 062B08 4880267 PAK pili- 062B09 3363603 PAK pili- 062B10 202392 PAK pili- 062B11 245488 PAK pili- 062C01 2796578 PAK pili- 062C02 1421710 PAK pili- 062C03 6193624 PAK pili- 062C04 4335461 PAK pili- 062C05 5582809 PAK pili- 062C06 1887384 PAK pili- 062C07 2674834 PAK pili- 062C08 3594859 PAK pili- 062C10 6126368 PAK pili- 062C12 6126368 PAK pili- 062D01 3063043<	062A08	245488	PAK pili-
062A12 245488 PAK pili- 062B01 5814642 PAK pili- 062B02 972216 PAK pili- 062B03 2482611 PAK pili- 062B04 3763613 PAK pili- 062B07 6163753 PAK pili- 062B08 4880267 PAK pili- 062B09 3363603 PAK pili- 062B10 202392 PAK pili- 062B11 245488 PAK pili- 062C01 2796578 PAK pili- 062C02 1421710 PAK pili- 062C03 6193624 PAK pili- 062C04 4335461 PAK pili- 062C05 5582809 PAK pili- 062C06 1887384 PAK pili- 062C07 2674834 PAK pili- 062C08 3594859 PAK pili- 062C10 6126368 PAK pili- 062C12 6126368 PAK pili- 062D01 3063043 PAK pili- 062D02 150387 </td <td>062A09</td> <td>245488</td> <td>PAK pili-</td>	062A09	245488	PAK pili-
062B01 5814642 PAK pili- 062B02 972216 PAK pili- 062B03 2482611 PAK pili- 062B04 3763613 PAK pili- 062B07 6163753 PAK pili- 062B08 4880267 PAK pili- 062B09 3363603 PAK pili- 062B10 202392 PAK pili- 062B11 245488 PAK pili- 062C01 2796578 PAK pili- 062C02 1421710 PAK pili- 062C03 6193624 PAK pili- 062C04 4335461 PAK pili- 062C05 5582809 PAK pili- 062C06 1887384 PAK pili- 062C07 2674834 PAK pili- 062C08 3594859 PAK pili- 062C10 6126368 PAK pili- 062C11 6126368 PAK pili- 062C12 6126368 PAK pili- 062D01 3063043 PAK pili- 062D02 150387<	062A11	4883451	PAK pili-
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088H04	648881	PAK
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120H09	3084423	PAK
120H11	481060	PAK
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149E08	2270211	PAK
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149F07	. 888188	PAK
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149F10	804821	PAK
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149G06	3900538	PAK
149G07	5293179	PAK
149G08	3177097	PAK
143000	1	

149G10	5134620	PAK ;
149G11	3348153	PAK
149H01 i	4108103	PAK
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149H03	4421910	PAK
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150C12	1991158	PAK
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150D07	6195267	PAK
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150E07	615432	PAK
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98414051	ygjD	Escherichia coli	580
90330537	surA	Escherichia coli	594
88262245	era	Escherichia coli	771
97295239	era	Salmonella typhimurium	. 771
97113525	tolQ	Pseudomonas aeruginosa	969
97113525	toIR	Pseudomonas aeruginosa	970
97113525	toIA	Pseudomonas aeruginosa	971
92355498	dapE	Escherichia coli	1162
95095976	flhA	Paracoccus denitrificans	1452
98414051	ycfB	Escherichia coli	1678
98429489	clpP	Caulobacter crescentus	1801
98429489	clpX	Caulobacter crescentus	1802
93224448	lon	Myxococcus xanthus	1803
99065127	lolA	Escherichia coli	2614
94110226	infA	Escherichia coli	2619 2981
98241618	lpxK	Escherichia coli	3107
91348525	metZ	Escherichia coli _{.c.} Escherichia coli	3107 3111
92193258	folC	Escherichia coli	3242
96405645	htrB	Escherichia coli	3625
95014035	surE	Escherichia coli	3653
94240115	frr	Escherichia coli	3654
93077430	smbA	Shigella flexneri	4043
96228708	ispA	Escherichia coli	4265
88163790 90264268	tufA rpoB	Escherichia coli	4270
96107188	lpxC	Escherichia coli	4406
84236117	ftsZ	Escherichia coli	4407
84236117	ftsA	Escherichia coli	4408
93003529	murG	Bacillus subtilis	4412
97361813	ftsW	Escherichia coli	4413
99047598	mraY	Escherichia coli	4415
99029898	rluD	Escherichia coli	4544
99000128	obg	Streptomyces coelicolor	4566
97284515	ispB	Escherichia coli	4569
93259941	murl	Escherichia coli	4662
91311678	infB	Escherichia coli	4744
92355498	dnaj	Escherichia coli	4760
92355498	dnak	Escherichia coli	4761
98414051	yjeQ	Escherichia coli	4952
96070892	kdtA	Escherichia coli	4988
96405645	msbA	Escherichia coli	4997
96347399	trxA	Synechocytis	5240
97177775	trxA	Rhodobacter sphaeroides	5240
93125123	polA	Streptococcus pneumoniae	5493
94012475	glmU	Escherichia coli	5552

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